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Robert O. Fisch, M.D.

January, 1980



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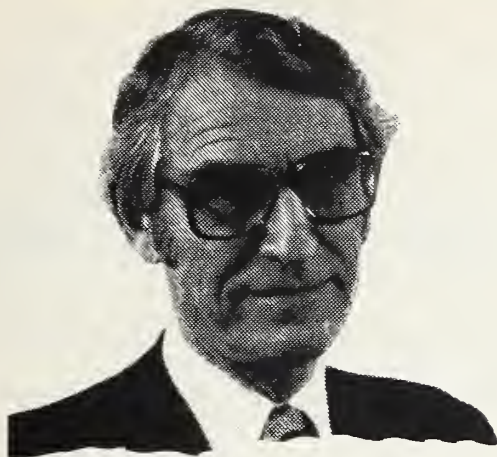


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## President's Letter

January being the first month of the new calendar year is a time when most of us, by custom, pause for reflection and a look to the future. As President of your MMA, I find myself doing just that.

It is apparent to me that there are so many areas and activities in which the Association could be legitimately involved, that we must immediately develop an improved mechanism for prioritizing our activities on the basis of cost benefit to the Association, its members, and our patients.

Our capabilities are limited by our income (primarily from dues, at this point). For this reason, membership recruitment and retention must continue to hold a high priority. Plans for a staff person devoted full time to this activity should go forward without delay. Creation of such a position will not, however, relieve us of an individual responsibility to advocate membership in the federation at all levels as we rub shoulders with our colleagues on a day-to-day basis.

As of this writing, it appears certain that by year's end, the Association will be settled in permanent housing shared with several affiliated and closely related organizations. Economic benefit in terms of stabilized rent and shared facilities are obvious and can be calculated. More difficult to measure, but equally if not more important, are the advantages of increased communication and cross fertilization of ideas between the various organizations.

The problems surrounding professional liability which appeared in this decade will assume increasing importance for each practicing physician as well as for society in general. The MMA has a continuing responsibility to be involved in study of the problem and to exert itself to protect the patient from injury due to malpractice, to defend members against unjustified claims, and to gain reasonable assurance that there is

value received for our premium dollar. It is my hope that all of us as individuals will become knowledgeable and actively involved in seeking a solution to this problem.

Health planning by government agencies continues apace. The Physician's Health Task Force, conceived, organized and directed by Dr. John Coleman and MMA staff, has gained increasing credibility and influence in local health planning and has become a model for the nation. This has been a major achievement of the Association, the importance of which cannot be over-estimated. Thus, we have done well over the short course. It remains to be seen, if we have the stamina and will for the long pull. Other members must take up the burden with renewed dedication and vigor.

To be adequate to the challenge of the future, MMA will require dedication from a loyal staff, the acknowledged talents and energies of whom will need to be wisely directed and efficiently used. The staff, in turn, must be undergirded by strong support and clear, firm direction from the membership through its leaders.

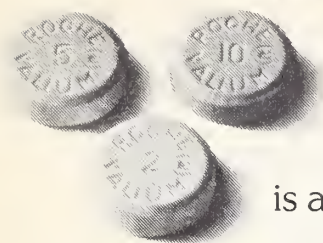
Your House of Delegates and Board of Trustees have become increasingly knowledgeable and able to deal in an objective and business-like fashion with difficult matters which often require painful decisions. The health and strength of our organization depends upon the willingness of our leadership to make those difficult decisions. I believe that we are equal to it.

Let each of us resolve to do our part to insure that the Association moves forward into the 80s with confidence and strength.

Frank E. Johnson, M.D.  
President  
Minnesota Medical Association



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Valium (diazepam/Roche) is a benzodiazepine with a character all its own.

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The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

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**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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## Editor's Notebook

### An Unhappy Fairy Tale

*'The best-laid schemes o' mice an' men  
Gang aft a-gley,  
An' leave us nought but grief and pain,  
For promised joy!'*

Robert Burns  
"To A Mouse"  
Scottish Poet, 1759-1796

Edinburgh, Scotland — This is a fairy tale setting.

I am sitting in a second-floor hotel room in the Hotel Caledonia. As I gaze through the window, I view Princes Street, one of the more picturesque shopping promenades in Europe. In the distance loom two monuments. One is for Sir Walter Scott, the Gothic novelist who wrote *Ivanhoe*. The other is for Robert Burns, Scotland's renowned poet. Across the street, beautiful gardens and a park parallel Princes Street. To the right, Edinburgh Castle, a fairy tale castle if there ever was one, towers over the hotel and the city. Even the name of the hotel, "Caledonia," has a fairy tale quality. It isn't "Camelot," but it's close enough. As long as I'm in this fairy tale mood, perhaps I shall tell one.

#### A Fairy Tale

*Once upon a time, not so many years ago, an Island Nation lay prostrate after a Great World War. Island citizens — weary of strife, improverished, exhausted, and nearly destitute — voted to reject the philosophy of their war leader. This bulldog of a man preached self-reliance, courage, tenacity, and individualism. These qualities, the citizens decided, might be good for war, but not for peace. Instead of individualism, there would be collective pooling of decisions, wisdom, and resources. Because of the perfectibility of man, equality and harmony would reign.*

*Their war leader warned them of their folly.*

*"I do not believe in the power of the state to plan and enforce. No matter how numerous are the committees they set up or the ever-growing hordes of officials they employ or the severity of the punishments they inflict or threaten, they can't approach the high level of internal economic production achieved under free enterprise.*

*Personal initiative, competitive selection, the profit motive, corrected by failure and the infinite processes of good housekeeping and personal ingenuity, these constitute the life of a free society. It is this vital creative impulse that I deeply fear the doctrines and policies of the socialist government have destroyed.*

*Nothing that they can plan and order and rush around nor forcing will take its place. They have broke the mainspring, and until we get a new one, the watch will not go. Set the people free — get out of the way and let them make the best of themselves.*

*I am sure this policy of equalizing misery and organizing scarcity instead of allowing diligence, self-interest and ingenuity to produce abundance has only to be prolonged to kill this British Island stone dead.”<sup>1</sup>*

*He spoke well, as a Prime Minister should*

*But the citizens did not listen. They would achieve social justice, equality, and security through central planning. One of their great economists, who was later to win a Nobel Prize, predicted social planning would endanger freedom, and would be the road to serfdom.*

*Still they did not heed. The new leaders nationalized factories, trains, and mines. But their greatest gift to themselves was Free Health Care: Ah, what a beautiful word — “Free”. Therefore no one need worry.*

*Embarrassing questions, such as “who can pay?”, “who shall go to the hospital?”, or “who shall live?”, need not be asked. Now one could simply ferret out those patients with sickness, care for them, and cure them.*

*There would be less sickness, financial burdens would be lifted, and all would be well. Free care would be brought within reach of the whole population. The care would be universal, comprehensive and without charge. It would be an act of pure generosity — of entitling people to their right of health.*

*Only a few details needed to be worked out: (1) nationalizing all hospitals, (2) making all doctors government employees; and (3) organizing the system. The latter would be easy. Separate free care into three parts — a hospital service, general practitioners service, and a public health service.*

*But details would not matter, for given the perfectibility of collective leadership and the citizens’ desire to work for the common good, a Great Plan would evolve.*

*This Plan would be rational, comprehensive, organized, coherent, equitable, and systematic, rather than being left to the vagaries of individualism or to the market place. All collective problems, in short, would be handled rationally for the common good with complete foresight. And then citizens would live happily ever after in good health.”*

### **A Week in Scotland**

Or at least that is the way it was supposed to be. After spending a week here — visiting hospitals, reading Scottish newspapers, perusing British books and the health system, talking to patients and doctors, and watching the televised proceedings of the Conservative Party Conference — In Blackpool, England, I think I can safely say: (1) something has gone wrong with the fairy tale; and (2) health planning is not what it was cracked up to be. As an American physician who believes that no amount of government planning can match the flexibility, choice, and quality of a mixed health system, with a dominant place for private practice, I am hardly an unbiased observer of the health scene here.

### **Observations on System**

Yet, I am sure enthusiasts and critics would agree on these observations on the National Health System:

1. Central health planning has unforeseen consequences. Instead of lessening the demand for health services, the demand has increased enormously — so much so that rationing must accompany “free” health care. This rationing applies particularly to elective surgery, which has waiting lists of months to years. The waiting list for hernias, hemorrhoids, gallstones, hip replacements, varicose veins, and tonsillectomies has grown by 40 percent in the last two years and now includes almost over 750,000 people.<sup>3</sup> Because of increased demand, the cost (\$18 billion a year) of the NHS strains the national budget and has resulted in either cutbacks (i.e. hospital building) or charges for services (i.e. dental services and spectacles).



2. A government health service can never be totally comprehensive. This lack of comprehensiveness goes beyond elective surgery. For example, the National Health Service does not provide routine physicals, most nursing home care for the elderly, screening for disease, or enough abortion services (private practitioners perform 60 percent of abortions).

3. Private health care is growing in Britain. Two and one-half million citizens belong to private health plans; unions and corporations (Electrical and Plumbers Trade Union, Birmingham brewery workers, London taxi drivers, and IBM employees) have private health plans as a fringe benefit; and the number of private hospitals, now 117, is growing at 10 percent a year.<sup>3</sup> To help the private health care along, the Conservative government is going to make private health care benefits tax deductible.

4. Most of the people like the National Health Service, yet most of the physicians dislike it. This should come as no surprise, since any "free" government health service inevitably is a politician's dream and a physician's nightmare. Poll after poll indicates the British public likes the idea of accessibility to general practitioners and the absence of worry of hospital costs. The English, who have had "to make do" and "queue up" for forty years, are not concerned about quality or efficient care. The following passage, from the *Changing National Health Service*, a book that favors NHS, nicely sums up patients' attitudes:

"The general public like the NHS. But since their attitude is so very unsophisticated, it is not very clear what is liked. It does not seem to be modern efficient care. Most patients seem to be more concerned with externals like communication, friendliness, accessibility and physical comfort than with the quality of examination and treatment. It follows that most patients do not know what is good for them in a medical sense."

As for doctors, their morale is low. As Powell, the Minister of Health in 1966, said, "One of the most striking features of the National Health Service is the continual, deafening chorus of complaint which rises day and night from every part of it. It is a unique spectacle of an undertaking that is run down by everyone engaged in it."

Most of the funds of the service go to hospitals, and therefore the general practitioners, who do not do any work in hospitals, are cut off from training, facilities, and professional stimulus. General practice, particularly in rural Britain, has little appeal, and London has three times more than outlying regions. The lot of the consultant, who works in a hospital is better but not much, for consultants must participate in the bureaucratic decision making. Pay for the average physician is low, less than three times that of a manual laborer, and somewhere between one-third to one-half of European, Canadian, or American counterparts. As a consequence, more physicians are joining Unions and are demanding shorter working hours.

Physician emigration rates are high, as many as 30 percent of physicians trained in England's medical schools practice abroad.<sup>5</sup> Who replaces these physicians? Indians and Pakistani physicians comprise 75 percent of hospital junior staffs and fill the ranks of general practitioners.

5. The public and the profession have different expectations of what the Service should provide. The public wants amiability, accessibility, and conveniences, and physicians desire better facilities, more sophisticated diagnostic equipment, freedom in decision making, and more efficiency and effectiveness in putting their training to good use. These different expectations led to bureaucratic and managerial conflicts. Physicians feel committee work is a waste of their skills and lowers the quality of care by diminishing the quantity of time devoted to it. Many of the bureaucrats, on the other hand, feel that equality, not quality, is what counts.

These differences in goals led to frequent "directives" to doctors from the Health Ministry. The intent of these directives was to force physicians to comply with the rules. Instead they led to delays, to inefficiencies, and to reorganizations to correct these inefficiencies. By the early 1970s, 625 different organizational bodies, ranging from

regional hospital boards to local health authorities, each with overlapping boundaries of authority and geography, were trying to run the Service. In 1974 the Service was reorganized into 90 area health authorities (AHAs), each responsible for "meeting the total health needs of a defined population".

In addition, this reorganization supposedly unified the hospital, physician, and public health services. This all sounds plausible, but the Service is continuing to suffer a succession of labor disputes, budget restraints, and managerial crises. These events not only remind me of Churchill's words, quoted earlier, but of those of Milton Friedman, the Conservative economist:

"Government can never duplicate the variety and diversity of individual action. At any moment of time, by imposing uniform standards in housing, or nutrition, or clothing, government could undoubtedly improve the level of living of many individuals; by imposing uniform standards in schooling, road construction, or sanitation, central government could undoubtedly improve the level of performance in many local areas and perhaps even on the average of all communities. But in the process, government would replace progress by stagnation; it would substitute uniform mediocrity for the variety essential for that experimentation which can bring tomorrow's laggards above today's mean."

In Britain's National Health Service, a kind of *paralysis by analysis*, and *planning for stagnation* has set in. Every one, of course, has to be a planner to some degree and no one can object to planning in a general sense. But what planners fail to mention is that planning too often is done by those removed from what they are planning, and by those who fail to realize individual creativity, innovation, and choice are necessary for excellence. Too often, "planning" is a euphemism for regulating, controlling, and rationing resources and services through committees, forms, and procedures. Too often, planners neglect results, consequences and quality. Instead of achieving equity and access, they commit society to, at best, a competent mediocrity.

6. Hospitals are deteriorating. Fifty percent of British hospitals are of pre-1918 vintage, and more than 70 percent are pre-1948. Even though 55,000 beds were replaced between 1966 and 1975, only a quarter of the total beds are in post-World War II buildings. Hospital construction is now almost at a halt. Even at the peak of building activity, 1966 to 1975, beds were only being replaced at a rate which would have allowed replacement every 55 years.

7. Government health plans, once instituted, are difficult to change. The new Prime Minister, Margaret Thatcher, has introduced these general policies — tight monetary control, reduced government spending, cutting income taxes, raising sales taxes, and reducing government health and welfare services. She plans to do the latter by reducing welfare benefits, by cracking down on foreigner's use of the NHS, by closing marginal hospitals, by abolishing one of "tiers" of hospital administrators — the local health authorities, by reducing paper work, by reversing the trend towards centralized hospitals, by abolishing maternity grants, by raising pension age for women from 60 to 65, and by having employers pay for the first six weeks of employees' sickness benefits. The Conservative government may cut 10,000 to 20,000 administrative positions from the Service. According to Conservative Michael Carter, "the service has grown fat on an administrative bureaucracy, which instead of getting to grips with its problems, occupied itself with the reorganization of inefficiency."

Will the Health Service be cut? I'm doubtful. To talk in the United Kingdom of cutting health services is still tantamount to questioning the virtue of the Queen. The National Health Service is the jewel in the crown of socialism, and, as the labor party spokesmen are fond of saying "must not be dismantled." When Margaret Thatcher raises the prices for dental fees or spectacles, or when she threatens to close day-care centers, she is disdainfully denounced as "Atilla the Hen", presumably because she is disturbing the pecking order of



the Health Service bureaucracy.

8. The problems of the National Health Service cannot be considered apart from the "English disease" — lack of productivity. Lack of productivity has many roots: Too much state intervention. Expensive welfare programs. Heavy tax burdens (the government takes 60 percent of national income). Low income (only one percent of Britons earn over \$14,000 while the U.S. median income is \$13,000). Strident trade unionism. Lack of incentives (the government confiscates 98 percent of profit). These policies shrink the national income and produce stagnant growth. Little money remains for the Health Service. Trade unions aggravate the productivity problem. At one point a year or so ago, ambulance drivers, orderlies who wheeled patients to surgery, and nurses were on strike. Because of frequent strikes, it sometimes takes seven to ten years to build a hospital. In one hospital I visited, laboratory computer programmers left in a pay dispute three years ago and never returned. Add to these policies and problems an inflation rate of 17 to 20 percent, and you can see why stagnation and drifts that beset the national economy drag down the health system.

### Lessons for America

Are there lessons for America? A couple. One, don't expect too much from PL-93-641 — the law passed by Congress in 1974 that set up the 205 Health Service Areas (HSAs) in the U.S. Centralized or regional health planning can never efficiently replace local market forces. At least, that law acknowledged that health reform could not be done by government alone since it calls for participation by many non-government groups. Two, maybe America has been smart to have the long debate and delay of National Health Insurance. We have had the opportunity to look more deeply into our own experience with government health programs and to the experiences of other governments. Now, even passionate liberals have discarded thoughts of complete reliance on the public medical service approach. Skepticism grows among the public about government's ability to deliver on its promises. If my experiences on my recent Scotland trip and on my other four trips to the United Kingdom are any barometer, the public has good reason for its skepticism.

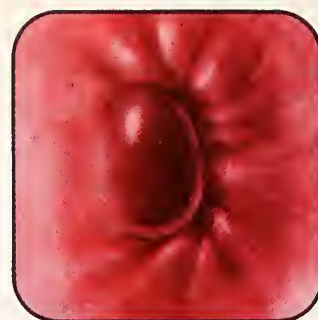


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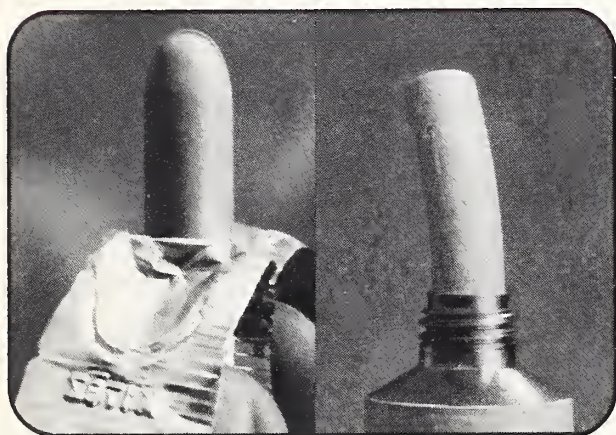
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**Description:** Each Anusol-HC Suppository contains hydrocortisone acetate, 10.0 mg; bismuth subgallate, 2.25%; bismuth resorcin compound, 1.75%; benzyl benzoate, 1.2%; Peruvian balsam, 1.8%; zinc oxide, 11.0%; also contains the following inactive ingredients: bismuth subiodide, calcium phosphate, and certified coloring in a hydrogenated vegetable oil base.

Each gram of Anusol-HC Cream contains hydrocortisone acetate, 5.0 mg; bismuth subgallate, 22.5 mg; bismuth resorcin compound, 17.5 mg; benzyl benzoate, 12.0 mg; Peruvian balsam, 18.0 mg; zinc oxide, 110.0 mg; also contains the following inactive ingredients: propylene glycol, bismuth subiodide, propylparaben, methylparaben, polysorbate 60 and sorbitan monostearate in a water-miscible base of mineral oil, glyceryl stearate and water.

**Indications:** Anusol-HC Suppositories and Anusol-HC Cream are adjunctive therapy for the symptomatic relief of pain and discomfort in: external and internal hemorrhoids, proctitis, papillitis, cryptitis, anal fissures, incomplete fistulas and relief of local pain and discomfort following anorectal surgery.

Anusol-HC Cream is also indicated for pruritus ani. Anusol-HC is especially indicated when inflammation is present. After acute symptoms subside, most patients can be maintained on regular Anusol<sup>®</sup> Suppositories or Ointment.

**Contraindications:** Anusol-HC<sup>®</sup> Suppositories and Anusol-HC<sup>®</sup> Cream are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

**Warnings:** The safe use of topical steroids during pregnancy has not been fully established. Therefore, during pregnancy, they should not be used unnecessarily on extensive areas, in large amounts, or for prolonged periods of time.

**Precautions:** Symptomatic relief should not delay definitive diagnoses or treatment. If irritation develops, Anusol-HC Suppositories and Anusol-HC Cream should be discontinued and appropriate therapy instituted.

In the presence of an infection the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Core should be taken when using the corticosteroid hydrocortisone acetate in children and infants.

Anusol-HC is not for ophthalmic use.

**Dosage and Administration:** Anusol-HC Suppositories—Adults: Remove foil wrapper and insert suppository into the anus. One suppository in the morning

and one at bedtime, for 3 to 6 days or until inflammation subsides. Then maintain patient comfort with regular Anusol Suppositories.

Anusol-HC Cream—Adults: After gentle bathing and drying of the anal area, remove tube cap and apply to the exterior surface and gently rub in. For internal use, attach the plastic applicator and insert into the anus by applying gentle continuous pressure. Then squeeze the tube to deliver medication. Cream should be applied 3 or 4 times a day for 3 to 6 days until inflammation subsides. Then maintain patient comfort with regular Anusol Ointment.

**NOTE:** If staining from either of the above products occurs, the stain may be removed from fabric by hand or machine washing with household detergent.

**How Supplied:** Anusol-HC Suppositories—boxes of 12 (N 0047-0089-12) and 24 (N 0047-0089-24); in silver foil strips with Anusol-HC W/C printed in black.

Anusol-HC Cream—one-ounce tube (N 0047-0090-01); with plastic applicator, detachable label.

Store between 15°-30° C (59°-86° F)

Full information is available on request.



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AN-GP-91

## The professional source of anorectal comfort



# Ultrasound of Renal Transplant Complications with C.T.\*

## Correlation in Selected Cases

DENNIS G. SCHOLL, M.D.† and SAMUEL B. FEINBERG, M.D.††

The renal transplant recipient may encounter many possible complications both immunological and surgical. Allograft rejection and urologic complications resulting in abnormal fluid collections (lymphocele, abscess, hematoma or urinoma) and obstruction of the ureter may have similar clinical features. The early, accurate diagnosis of these entities can expedite appropriate medical and surgical management. The non-invasive nature of ultrasound and computed tomography make these modalities particularly suited to this end. Our ultrasound findings and early C.T. experience in this clinical situation are presented.

**R**ENAL TRANSPLANTATION has become an established procedure in numerous centers throughout the country. It has been responsible for the stimulation and development of a great volume of basic and practical immunologic knowledge. From the point of view of the day-to-day management of transplant patients, simple, safe and non-invasive techniques are desirable to detect early signs of complications arising from transplantation. It is not the purpose of this report to recapitulate the vast immunologic, chemical, and nuclear radiology literature in the study of the renal transplant status. Instead, we wish to describe the ultrasound appearance of several complications of renal transplantation which we have encountered. Computed tomographic evaluation of the transplant patient is a more recent diagnostic procedure at our institution and correlation with ultrasound findings in several patients is included.

### Methods

Nine hundred patients have received renal allografts at the University of Minnesota Hospitals from 1963 through 1976. Until 1976, the patients had not been referred for ultrasound examination as a routine part of the rejection evaluation protocol. Statistical analysis of our cases is not presented because, for the most part, the examinations have been done to evaluate clinically suspected masses or obstruction. Recently, the trend has been to expand its use in the evaluation of rejection

as well. In the last six months of 1976, seven patients had computed tomography (C.T.) correlation of ultrasound findings. The ultrasound and C.T. findings described below are from this group of patients.

Ultrasound examinations were performed using commercial equipment with grey scale, bistable, and A-mode capabilities as displayed on cathode ray tube and video scopes. 1.6, 2.25 and 3.5 MHz focused transducers with 19 mm, 13 mm, and 13 mm diameters respectively, were employed. 70 mm roll film or Polaroid permanent images were obtained. C.T. scans were performed on an ACTA 0100 unit. Images from the video scope were recorded on Polaroid film. In these patients, intravenous contrast enhancement was

**TABLE**  
**Ultrasound Appearance of Renal Transplant Complications**

#### Allograft rejection

1. Halo of edema.
2. Indistinct collecting system-parenchyma acoustic interfaces.
3. Acute increase in renal volume

#### Urologic complications

##### Lymphocele

1. Pelvic or perinephric transonic mass.
2. Internal echoes develop if infected or contains clot.

##### Urinoma

1. Same ultrasound findings as lymphocele; usually paravesical.

##### Abscess

1. Complex, predominantly transonic, mass with internal echoes caused by septation and debris.

##### Hematoma

1. Transonic collection early; decreases in size and develops internal echoes as clot organizes.

##### Obstruction

1. Collecting system dilatation.

\*Technical support by Pfizer Medical Systems.

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See editorial page 36.



not employed.

### Ultrasound and C.T. Findings

We have divided our findings of renal allograft rejection and urologic complications in the Table.

#### Allograft Rejection

During rejection, swelling of the transplanted kidney resulting in an increase in volume has been described by Leopold<sup>1</sup> and Bartrum, et al.<sup>2</sup> Bartrum has indicated that an acute increase in volume of greater than 20 percent may be associated with rejection whereas, a slow increase in volume probably indicates hypertrophy. We do not routinely determine renal volume. Within the past six months, patients at our institution have been referred for serial ultrasound exams for evaluation of rejection. The diagnosis of rejection is suggested by the appearance of a "halo" of edema and we have also noticed that the acoustic interfaces between the parenchyma and collecting system of the kidney may be less distinct during an episode of rejection than in a stable state (Figure 1). Presumably this is also due to edema.

#### Urologic Complications

##### Lymphocele

Abnormal collections of lymphatic fluid may result from the disruption of the retroperitoneal or renal capsule lymphatics during transplantation surgery. Rashid,<sup>3</sup> has suggested that an antecedent hematoma creates a potential deadspace which allows the accumulation of lymphatic fluid and that the false capsule of the hematoma interferes with resorption. The resultant mass may cause symptoms related to



Fig. 1 — Longitudinal\* sonogram in a three-year-old girl who was clinically undergoing allograft rejection. Capsular and collecting system acoustic interfaces are indistinct and the renal parenchyma shows a transonic "halo" indicating edema.

\*The patient's head is to the reader's left in this and subsequent longitudinal sonograms.

compression of the kidney or ureter. As lymphatic fluid is an excellent growth medium for bacteria, an abscess may develop.

The usual ultrasound appearance is that of a perinephric or pelvic transonic mass (Figure 2). Internal echoes may be seen if the lymphocele contains clot or is infected. Diagnostic and therapeutic aspiration with ultrasound guidance has been reported.<sup>4</sup>

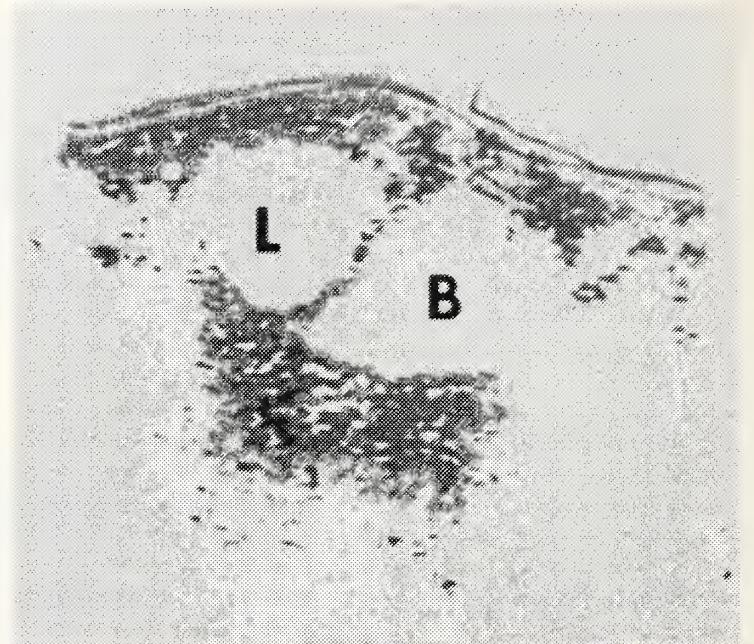


Fig. 2—Transverse sonogram† in a 43-year-old male shows a transonic lymphocele (L) impressing upon the right aspect of the urinary bladder (B). The patient had symptoms of mild rejection and a palpable right lower quadrant mass.

†The patient's left side is to the reader's right in this and subsequent transverse sonograms and C.T. scans.

While lymphangiography is the definitive study in the diagnosis of lymphocele, it is apparent that the true volume of the mass may not be fully appreciated as the oily contrast will pool in the dependent portion of the lymphocele. Moreover, if renal lymphatics are the source of the lymphocele, it will not communicate with the pedal cutaneous lymphatics which are cannulated during routine lymphangiography. C.T. examination may also show the presence of an abnormal fluid collection (Figure 3). In our experience to date, average ACTA numbers of lymphatic fluid do not differ significantly from urine and are, therefore, not helpful in determining the nature of the fluid collection.

##### Urinoma

Urine leakage following renal transplantation usually results from breakdown of the ureterovesical anastomosis or ureteral necrosis.<sup>5</sup> The extravasated urine may produce mass effect leading to obstruction and may become infected. The onset is variable but usually within six weeks following transplantation.<sup>6</sup>



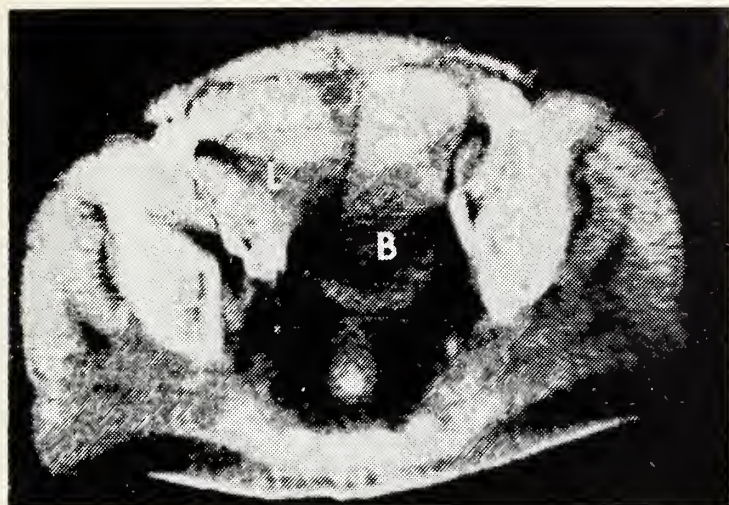


Fig. 3 — A C.T. scan in the same series as Figure 2 shows the lymphocele (L) indenting the bladder (B). The focal areas of increased attenuation in the dependent portion of the lymphocele are globules of Ethiodol, those to the right represent displaced lymph nodes.

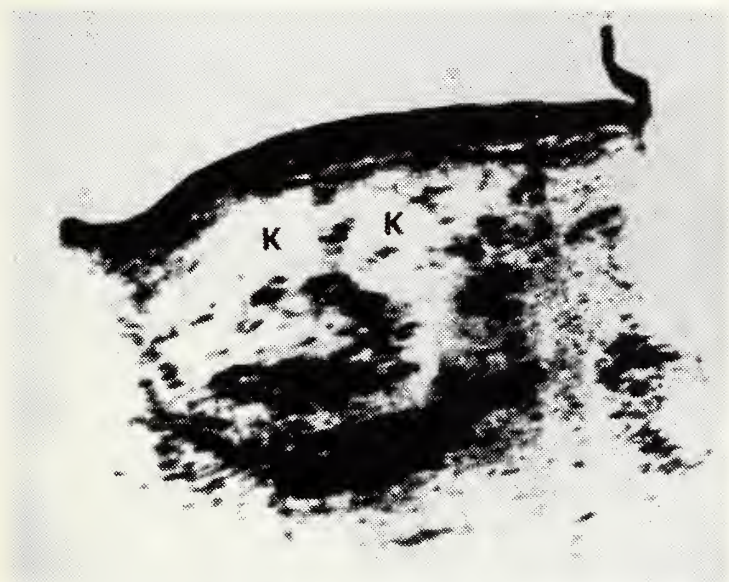


Fig. 4 — Transverse scan in a 30-year-old male who had received two infant cadaver kidneys (K) shows a large mass with a complex echo pattern interpreted to be either an abscess or an organizing hematoma. At surgery, a large perinephric abscess was drained.



Fig. 5 (a)—Transverse sonogram of the left upper quadrant in a 52-year-old male shows a predominantly transonic abscess.

Ultrasound shows a transonic mass, commonly in a paravesical or perinephric location. The appearance may be identical to that of a lymphocele and distinction may depend upon history. If the urine collection is infected, the appearance is that of an abscess (see below).

#### Abscess

Renal transplantation is usually preceded by splenectomy and bilateral nephrectomy. Abscess may occur, therefore, in the retroperitoneal or intraperitoneal spaces as a complication of these procedures. Following transplantation an abscess may also occur in the neoperinephric space.

A complex, predominantly transonic, mass is the usual ultrasound appearance (Figure 4). Internal echoes are caused by septation and debris within the abscess. The margins may be indistinct because of edema in the surrounding tissues.

An ultrasound exam (Figure 5 (a)) and a C.T. scan (Figure 5 (b)) of a patient with a subphrenic abscess following splenectomy showed a well defined, homogeneous mass in the left upper quadrant. The average attenuation coefficients of the abscess do not differ significantly from those of the liver and were therefore not helpful in determining the nature of the mass.

#### Hematoma

Hematomas may occur in the early postoperative period as a complication related to the vascular anastomoses. We have also seen intrarenal and extrarenal hematomas following percutaneous biopsy of the allograft done as part of the rejection evaluation.

Ultrasound examination of the acute hematoma



Fig. 5 (b)—A C.T. scan at the same time demonstrates the abscess (A). The area of increased attenuation medial to the abscess is the stomach which was opacified with orally administered contrast. The liver (L) is seen to the right.



shows a transonic collection. As the hematoma organizes it diminishes in size and develops internal echoes (Figure 6 (a) (b) ).

#### Obstruction

Obstruction of the transplanted kidney usually occurs because of stricture, ureterovesical anastomosis edema, calculus, or mass. The onset is variable depending upon the etiology.

Collecting system dilatation of various configurations is the usual ultrasound appearance of hydronephrosis (Figure 7). Sanders<sup>7</sup> has indicated that the size of the echo pattern correlates with the severity of the hydronephrosis while the shape does not.



Fig. 6 (a)—Transverse sonogram in a 27-year-old male shows a sonolucent hematoma (H) within the transplanted kidney. The scan was done one day following percutaneous biopsy of the kidney.



Fig. 6 (b)—One week later, the scan shows the hematoma to have decreased in size and internal echoes indicate organization of the clot.

#### Miscellaneous

In an additional case examined with the ACTA scanner, we have seen excessive intra-abdominal fat accumulation and irregular femoral heads indicating aseptic necrosis. Both of these findings were apparent on the radiographs of the abdomen and pelvis but present interesting C.T. findings. These are well known complications of the large doses of steroids that these patients commonly receive. The patient was examined because of the presence of a large lymphocele (Figures 8 (a) (b) (c) ).

#### Discussion

Allograft rejection is the most frequent complication that occurs in the renal transplant recipient. Starzyl indicated that rejection was the cause of renal failure in approximately 90 percent of his series.<sup>6</sup> Exclusive of the immune mechanisms resulting in rejection, deterioration of function in the transplanted kidney may be caused by many other factors. These have been termed urologic complications as they result from the surgery per se and usually require surgical correction.<sup>6</sup> These include hemorrhage, urine fistula, obstruction, lymphocele, and abscess. Malek, et al. reported a series of 1301 renal transplant patients in 1973.<sup>5</sup> Of these, 174 experienced urologic complications with 57 deaths attributed to these complications. Since the urologic complications are surgically correctable, it is important that their presence be determined early, and with as little intervention as possible, in the already stressed recipient.

Allograft rejection and urologic complications may present clinically as renal failure. Urine output,

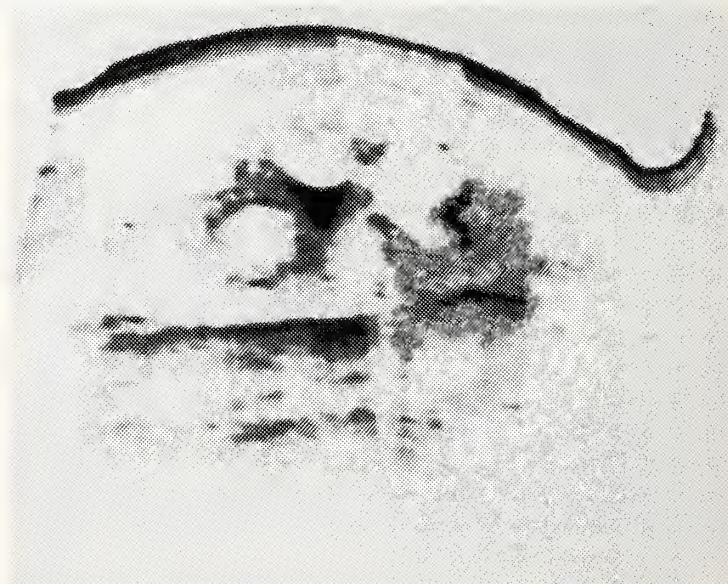


Fig. 7 — A longitudinal sonogram in a 24-year-old female demonstrates marked dilatation of the collecting systems. Complete obstruction at the ureteropelvic junction was confirmed with retrograde pyelography. Pyeloplasty was performed and renal function was restored.



temperature, and serum levels of potassium, BUN and creatinine may not be helpful in determining the etiology. Nuclear renogram may not enable one to distinguish acute tubular necrosis from rejection.<sup>8</sup> Other diagnostic modalities may be necessary.

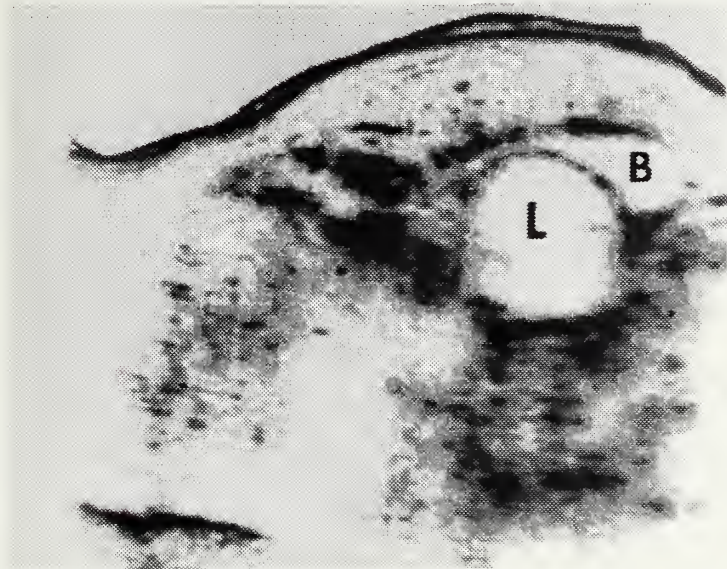


Fig. 8 (a)—A transverse sonogram of the pelvis in a 10-year-old girl demonstrates a sonolucent lymphocele (L) displacing the urinary bladder (B).

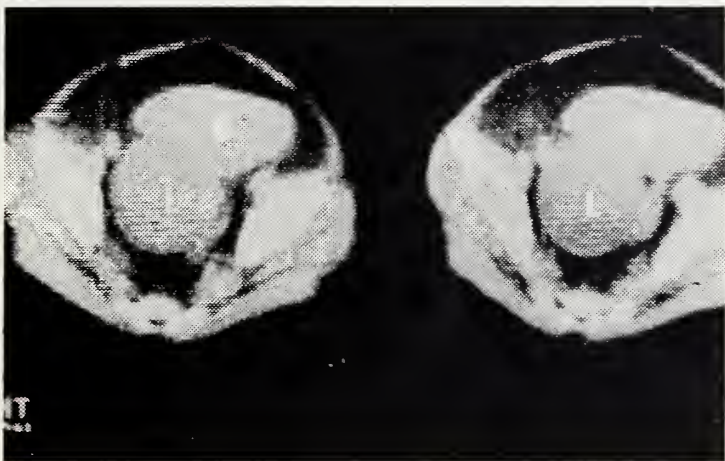


Fig. 8 (b) — A C.T. scan was done at the same level. Note the zone of decreased attenuation anterior to the bladder which represents intraabdominal fat. The patient was receiving steroid therapy and was clinically Cushingoid.

The first reference to the use of ultrasound in the evaluation of renal allograft rejection was by Leopold in 1970.<sup>1</sup> He described a method of determining renal volume as an indication of rejection. Since that time, ultrasound has also been shown to be an effective means of evaluation of urologic complications.<sup>3,9-13</sup> It can accurately assess the presence of the abnormal fluid collections resulting from abscess, hematoma, urine leak, or lymphocele and detect significant ureteral obstruction. The diagnosis of rejection can be aided by the ultrasound appearance of the transplanted kidney. Its non-invasive nature and ability to visualize the kidney, bladder, ureter, and perinephric soft tissues in spite of poor or absent renal function make ultrasound, in particular, ideally suited for the post-transplant patient in whom conventional excretory urography and lymphangiography may not be possible, and indeed, potentially harmful. Ultrasound is an established diagnostic modality. C.T. scanning offers a new, exciting, non-invasive imaging technique. Even though our experience with this modality is more limited, it is apparent that it will also aid in our ability to diagnose complications of renal transplantation.



Fig. 8 (c)—A C.T. scan at the level of the acetabulae in the same patient shows irregularity of the cortex of the right femoral head (arrow). This represents aseptic necrosis, a further complication of steroid therapy.

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**Contraindication:** Previous hypersensitivity to penicillin.

**Warnings:** Serious, occasionally fatal, anaphylactoid reactions have been reported. Some patients with penicillin hypersensitivity have had severe reactions to a cephalosporin; inquire about penicillin, cephalosporin, or other allergies

before treatment. If an allergic reaction occurs, discontinue the drug and treat with the usual agents (e.g., epinephrine or other pressor amines, antihistamines, or corticosteroids).

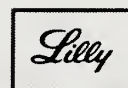
**Precautions:** Use with caution in individuals with histories of significant allergies and/or asthma. Do not rely on oral administration in patients with severe illness, nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility. Occasional patients will not absorb therapeutic amounts given orally. In streptococcal infections, treat until the organism is eliminated (minimum of ten days). With prolonged use, nonsusceptible organisms, including fungi, may overgrow; treat superinfection appropriately.

**Adverse Reactions:** Hypersensitivity, including fatal anaphylaxis. Nausea, vomiting, epigastric distress, diarrhea, and black, hairy tongue. Skin eruptions, urticaria, reactions resembling serum sickness (including chills, edema, arthralgia, prostration), laryngeal edema, fever, and eosinophilia. Infrequent hemolytic anemia, leukopenia, thrombocytopenia, neuropathy, and nephropathy, usually with high doses of parenteral penicillin.

[102175]

**\*Equivalent to penicillin V.**

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# History

## “The General”

### A History of Hennepin County Medical Center

#### Part I (of II parts)

TIMOTHY J. RUMSEY, M.D.\*

*“Men make buildings . . . then buildings make men.” – Winston Churchill*

**The evolution of Hennepin County Medical Center from a rented home to reconverted farm site to large metropolitan hospital is presented. Nuggets of medical history embellish the offering.**

WHEN FORMER Mayor George A. Pillsbury supported a resolution to establish a city hospital in 1887, the stage had already been set for public support of a medical center. It was not always so. In Minnesota's early days as a territory and a young state “one of its vaunted attractions for visitors and settlers was the alleged health restoring properties of its climate.”<sup>3</sup> Reports of Minnesota's wine-like air and magic ozone brought such notables as Henry David Thoreau, Clara Barton, and Dr. W. W. Mayo to the state in search of health.<sup>4</sup> Early citizens of Minneapolis capitalized on this idea and established many health resorts and healing springs. Incredibly, the city fathers actually felt “that the presence of physicians would damage the reputation of Minnesota as a health resort and strongly discouraged them at every opportunity.”<sup>5</sup> The *St. Paul Pioneer* supports this feeling in an 1850s article on Minneapolis which reads: “Physicians Mpls. does not want at all for any purpose, seeming to regard them as a fifth wheel of a coach in their profession and incorrigibly idle out of it.”<sup>6</sup>

The first practicing physician to establish an office in St. Anthony (Minneapolis' early counterpart) was John H. Murphy, who in 1850, formed a partnership with Dr. A. E. Ames shortly thereafter.<sup>7</sup> Dr. Murphy was known to be always prepared. If there was surgery to be performed, he would take out the spool of silk he carried with him, cut off a piece of suture, sharpen his knife on the heel of his shoe and say to the patient: “This is going to hurt like hell, but I can't help it, so look out.”<sup>8</sup>

Of all the early physicians in Minneapolis, Murphy's partner, Ames, was the most active in dealing with the “deserving poor”. In 1871, Dr. Ames and the Brotherhood of Gethsemane operated the city's first

out-patient clinic to supply the downtrodden “with medicine and advice gratis.”<sup>9</sup> In the same year, Ames and the Brotherhood, along with Bishop Knickerbacker, established the city's first hospital, known as the Cottage Hospital and later to be called St. Barnabas. This hospital started in a rented house on Washington Avenue. At this time there was also a so-called “pest house” outside the city limits, but until 1881 Cottage Hospital was exclusive in Minneapolis. It was said that “in that and the following years there was an epidemic of hospitals.”<sup>10</sup>

Most of the hospitals started in rented or donated homes. Their locations and dates of establishment



The old hospital with its cramped and vermin-infested rooms was so dreaded and abhorred by the general public that many a poverty-stricken patient preferred . . . the probably more wretched surroundings of his own home rather than brave the terrors which his own and his neighbors' imaginings had conjured up about the old institution.

\*St. Paul, Minnesota.





Brackett House, 1894



Hospital staff at Brackett site, 1901.



Minneapolis City Hospital, 1905.

follow:<sup>11</sup>

- 1882 — A. A. Ames Private Hospital  
Washington and Fourth Avenue South
- Minnesota College Hospital  
Bank and 2nd St. S.E. (formerly the Winslow Hotel)
- Sisters of Mercy  
6th St. and 25th Ave. South (later to be called St. Mary's Hospital and originally considered as a possible site for the first City Hospital)
- Homeopathic Hospital  
9th St. and 10 Ave. South
- Northwestern Hospital  
4th Ave. South and 25th St. (This institution was established for the treatment of women and children and its original staff was comprised wholly of women)
- 1886 — Maternity Hospital  
2215 Glenwood Avenue
- 1887 — Minneapolis City Hospital  
724 11th Ave. South

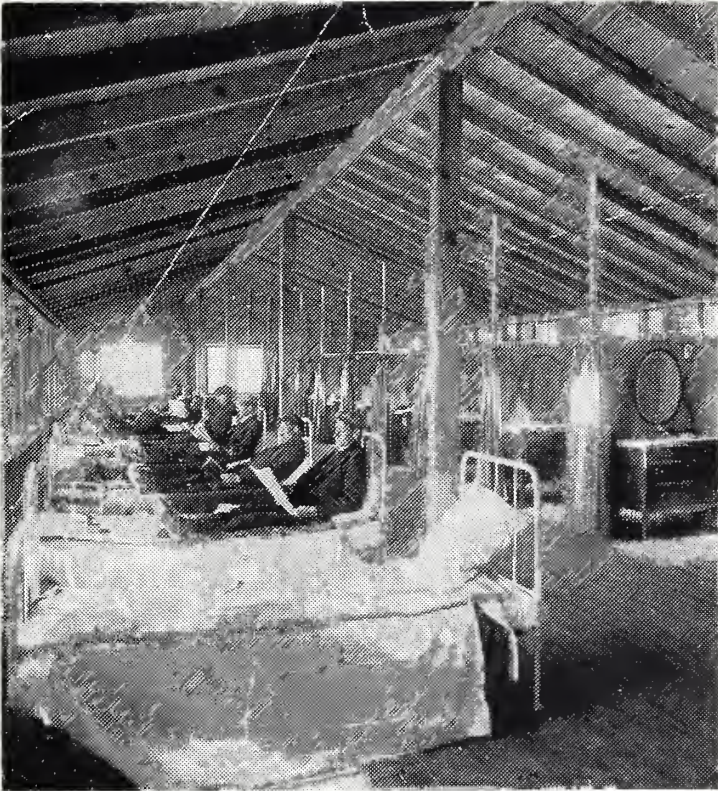
### City Hospital — The First Days

Prior to the actual establishment of city-operated hospital, the medical care of the poor came from several sources. The Brotherhood of Gethsemane operated a free dispensary as early as 1871. Private citizens underwrote some of the care the poor received in various hospitals, with the city picking up the bills somewhat later. In 1880, Dr. James H. Dunn was elected by the city council to care for “city cases” in private hospitals and in their homes. Dunn served several terms as city physician and eventually became the first superintendent of Minneapolis City Hospital.

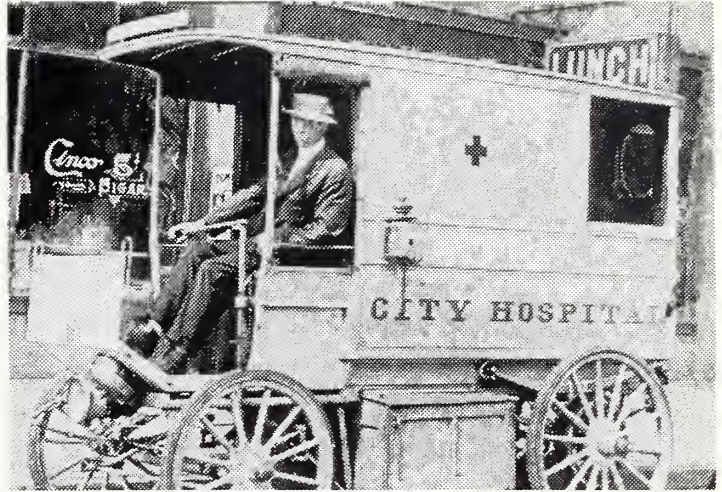
It soon became apparent that the existing system of a physician visiting patients scattered about the city was wholly unsatisfactory. Dr. Charles A. Chase reported to the city council that “We need a new City Hospital, and we trust the thought of farming (the sick) out to other hospitals has been settled forever.”<sup>12</sup> As mayor, George A. Pillsbury was instrumental in getting the wheels rolling for the establishment of a city run hospital. During the term of Mayor A. A. Ames, the hospital officially opened in September of 1887 in a rented home at 724 Eleventh Avenue South. Sixty-one patients could be accommodated at one time and were under the care of four nurses, a matron, two interns, and the City Physician who with an assistant continued to visit the sick cases outside the hospital. A general handyman cared for the premises. One hundred sixty-four people were treated in the first three months at a cost of eighty-four cents (84c) per person, per day. “Dr. Dunn could report as superintendent that the hospital was successful beyond his most sanguine expectations.”<sup>13</sup> To be sure, there were shortcomings despite his enthusiasm. Because of inadequate fire



“THE GENERAL” — RUMSEY



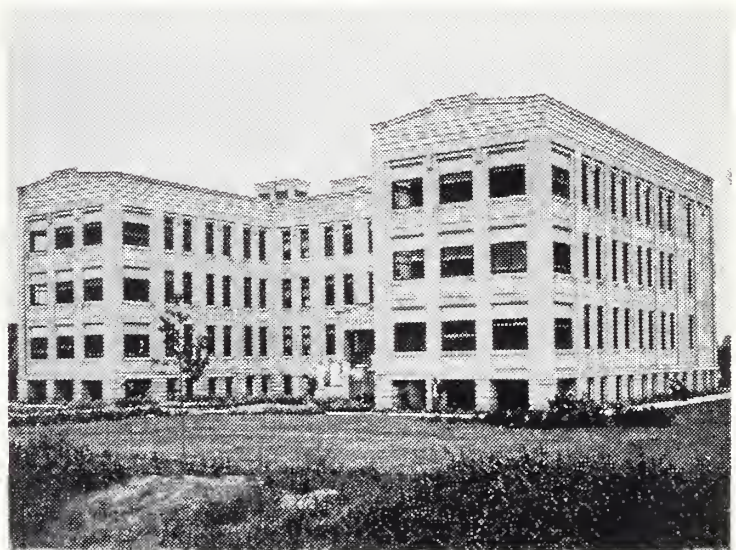
“Cottage” at Hopewell Hospital (later known as Parkview Sanatorium).



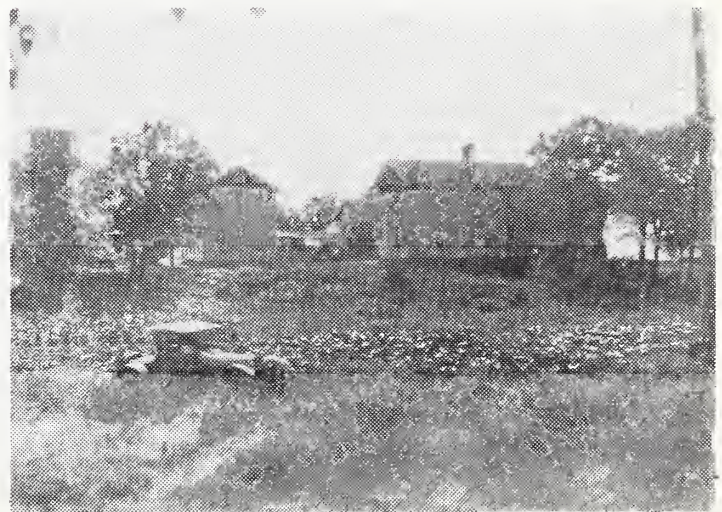
1910 — Herman Logan —  
First Power Driven Ambulance



Ward at Lymanhurst, 1918.



Hopewell T.B. Hospital, 1912



A contagion hospital located in St. Louis Park functioned through the 1920s.



protection, the employees had to be organized into a fire brigade to meet emergencies. The hospital quarters became a source of public reproach. Patients preferred to stay in their homes rather than go to the city institution. “The old hospital, with its cramped and vermin-infested rooms, was so dreaded by the general public that many a poverty stricken patient preferred . . . the probably more wretched surroundings of his own home, rather than brave the terrors which his own and his neighbors’ imaginings had conjured up about the old institution.”<sup>14</sup>

Between 1880 and 1890, the population of Minneapolis more than tripled from 47,000 to 165,000. A city hospital in a cramped, rented home was hardly destined to last. After only two years of operation in the rented quarters, hospital superintendent, Dr. Chase, recommended to the city council that immediate action be taken to secure suitably located grounds for a proper hospital building. In 1891, a specially created Board of Charities and Corrections was formed and one of its duties was to manage the hospital. This body was the forerunner of the Board of Public Welfare which was to assume similar duties in 1920. The initiation of a twenty-five thousand dollar bond allowed the Board of Charities to commence acquiring the property for a new hospital. (It is noted that the bond issue of 1969 for the new Medical Center would be for twenty-five million dollars.) The Regents of the University of Minnesota formally asked that the hospital be located in close proximity to the school for the benefit of both parties. An alternate site would be chosen, but a vital

relationship between the two institutions has been maintained to the present.

In June of 1893, the farm property and buildings bounded by what is now 6th and Portland and 5th and Park Streets were purchased from former Mayor George A. Brackett for \$100,000. The existing structures consisted of a large brick house, a spacious frame stable, and three frame houses. Remodeling began at once.

### The Second City Hospital Opens

After four months of converting the structures for hospital use, the patients were moved from the original rented quarters to the new facilities. This was completed by October 31, 1893. Mr. Brackett’s home was used as the main building, which contained the office, three medical wards, a general dining room, and four sleeping rooms for the household workers. The fifty-nine beds in this building were for males only. Twenty-four beds for females were placed in one of the frame buildings and a small cottage housed twelve contagious disease beds. The remaining frame structure was fitted up for the matron and her charges and became the first Nurses’ Home. A new one-story brick building contained the boiler and engine room and coal bins in the basement, with a first floor laundry and kitchen. The stable became the dispensary with the horse stalls converted to exam rooms and the harness room was turned into a pharmacy. All the buildings, except the “contagious” cottage, were connected to



From the occupancy of the Brackett site in 1893 until the opening of the modern day Hennepin County Medical Center in 1976 the hospital was always a collection of piecemeal fashioned structures.



each other by an eight foot hallway.

Dr. Charles Weston, in his annual report for the first year in the new quarters, referred with satisfaction to the fact that in these buildings they had an unfailing supply of hot water. This was a source of gratification to those who had worked in the old hospital where it could often be had only in “tea-kettle lots.”<sup>15</sup> The remodeled buildings served well for some time but were torn down to give way to the more permanent buildings which would become what we know as “The General”.

### Expansion — The Ever Present Need

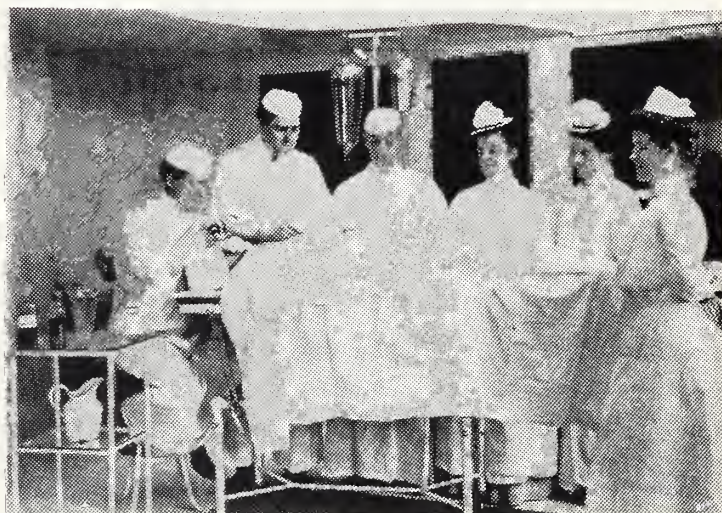
Ever since the original City Hospital treated the first patient, it and its successors were haunted by inadequate facilities and the need for expansion. Only one year after the hospital on the Brackett property opened, twenty-two patients had to be sent to private hospitals. During the typhoid fever epidemic of 1894, two tents were put up on the hospital lawn to accommodate twenty overflow patients. Dr. Weston, the superintendent, felt that this outdoor treatment of fever cases was of great advantage to them. These benefits, notwithstanding, Dr. Weston became instrumental in expanding the physical plant which would eventually include off hospital sites as well.



Corridor in the Contagious Building, 1916.

### Expansion Chronology

- 1887 — First Hospital,  
724 Eleventh Ave. So.
- 1893 — Second Hospital,  
Brackett property
- 1898 — Outpatient Building
- 1901 — East Wing
- 1908 — Hopewell Hospital (T.B. Center in North  
Minneapolis later named Parkview in 1920)
- 1913 — Lymanhurst Pediatric Unit,  
Chicago Ave. & 18th St.
- 1914 — West Wing
- 1918 — Contagious Building (later named Annex in 1945)  
Administration Building/Nurses Home — Laundry
- 1922 — Marcy School Site (chronic patients were housed in this  
vacant building near the main hospital)
- 1933 — Norman Hotel (rented for Nurses Home),  
712 So. 5th St.
- 1944 — Harrington Hall addition (named in honor of former  
superintendent, Dr. F. E. Harrington)
- 1949 — Expansion of the Annex Building
- 1958 — Medical Research Laboratory
- 1962 — Outpatient Mental Health (space rented in  
McGill Bldg.)



Minneapolis City Hospital Operating Room — Surgery Team 1916.



Dietetic laboratory — eighth floor — Nurses' Home, 1918.



**Expansion Chronology (continued)**

- 1970 — Family Practice Clinic
- Emergency Room expansion
- 1976 — New Hennepin County Medical Center opens

It is noted that the buildings erected at the main hospital site between 1898 and 1918 completed the essential form of “The General” which would function up to moving day of 1976.

By 1920, the total bed capacity was 685 (including the branch hospitals, Hopewell and Lymanhurst) and it had gained an excellent national reputation. In 1921, it received a class A rating from the American College of Surgeons and it also earned approval by the American Hospital Association in the following year. A *LIFE* magazine article, with photographs by the famous Alfred Eisenstadt, brought “The General” into millions of American homes in 1941.

**1937 Superstructure To Meet Needs  
for Several Centuries**

It came as no surprise to the hospital staff that a 1926 Minneapolis Grand Jury report felt the hospital was overcrowded. One year later, overflow patients were still being sent to private institutions and in 1929, forty-one thousand dollars would be spent “farming out” city patients. The outpatient department bore the burden also and was reported to be “desperately overcrowded and in need of additional floor space unless it is to become a menace rather than a benefit.”<sup>16</sup> For several years, city planners worked with the hospital staff and in 1935 presented a plan they felt would be “ample to the needs of the community for several centuries.”<sup>17</sup> It was to be a 23-story “modern hospital structure” facing Portland Ave. and situated between the annex and the administration building. They extolled the virtues of this plan on the basis of “modern hospital construction (tending) toward the perpendicular rather than horizontal (and) patients are thus farther removed from the dust and noises and odors of modern industry; and the air they breathe is purer and cleaner (and) is said to contain a much higher quotient of oxygen and less carbon monoxide and other injurious gases.”<sup>18</sup>

Constant funding shortages stymied these plans and the last significant expansion at the General was the addition of improvements to existing structures and the construction of the Medical Research Lab and Family Practice Clinic.

**Expansion To Other Sites**

Early typhoid, diphtheria, and scarlet fever epidemics were continually forcing an overflow on the hospital as

already noted with the erecting of tents on the hospital grounds in 1898. Many off-hospital sites would be used to compensate. In 1914, two vacant houses on the campus of the University of Minnesota had to be utilized for contagious patients. In 1922, thirty-five “chronic” patients were housed in the Marcy School (an unused building near the hospital) for several years to make way for acute cases at the main hospital.

As early as 1908, Mr. and Mrs. William R. Dunwoody had deeded eight acres of land in North Minneapolis (Camden) to be used for hospital purposes. A frame cottage was erected on the site which happened to be next to the old workhouse. This building became the start of Hopewell Hospital, the city’s first tuberculosis treatment center. A new structure was completed four years later by the workhouse inmates, thus, adding 100 beds to the total hospital capacity. The first floor of Hopewell was given over to chronic patients, some of whom had been residents of the Marcy School Annex. The remainder of the new brick building was then occupied by the TB patients, many of whom had been on a waiting list for months.

With the expansion of Hopewell, the bed capacity of City Hospital was nearly 700. Hopewell would



“The General”



become Parkview Hospital in 1920, and sustained its previously mentioned function until 1924 when all TB patients were transferred to the Glen Lake Sanatorium. Parkview then housed 170 beds for chronic patients who were mostly mentally ill and incurable.

In its early years, City Hospital had always been short of beds for children. In the summer of 1908, another tent was erected in the hospital yard as a children's ward. Here, five times as many children were cared for during that summer as had received treatment in any of the preceding five years. In October, the children had to be moved back into the overcrowded hospital. Two prominent Minneapolis citizens, George and Frederick Lyman, knew of this dilemma and donated their homestead to the city for use as a children's hospital in 1913. This property, located on Chicago Ave. and 18th St. consisted of "two well preserved dwellings set in large lawns in a favorable location."<sup>19</sup> One building was made suitable as a hospital which could accommodate 65 to 70 children. The other building was to be used as a nurses' and employees' home. The hospital building proved inadequate and construction of a new building began in 1917, but this was halted because of insufficient funds.

In October of the following year, the children were transferred back to the main hospital. The proposed building, Lymanhurst, was finally opened, but expenses and insufficient staffing allowed it to operate as a children's hospital for only a few years (1922-1926). It then functioned solely as a pediatric tuberculosis out-patient clinic until 1931, when Lymanhurst School for Tuberculosis Children was established on the recommendation of Dr. F. E. Harrington. Several years later, the name was changed to Lymanhurst Health Center and its services included adult and pediatric TB clinics, a venereal disease clinic, a cardiac clinic, and a convalescent home for approximately forty children with rheumatic fever.

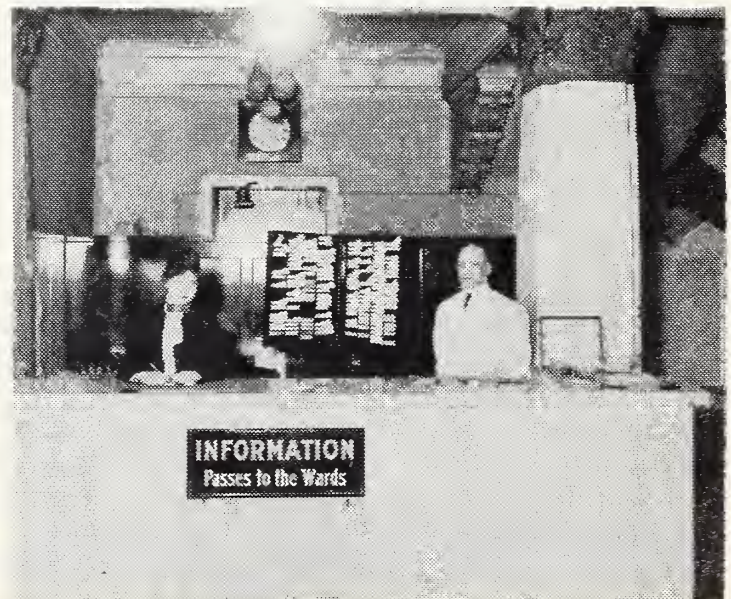
In actuality, the City Hospital had no management connections with Lymanhurst after 1927, although its medical staff were in attendance. Most notably was Dr. J. Arthur Myers, who served as Chief of Medical Staff for twenty years.<sup>20</sup> On December 17, 1942, the City of Minneapolis Public Welfare Board dedicated the former Lymanhurst facilities to the Elizabeth Kenny Institute. Dr. Harold S. Diehl, Dean of the Medical Sciences at the University of Minnesota, addressed the audience gathered to honor Sister Kenny (the Australian "out-back" nurse) whose world renown began with recognition of her treatment of polio at the Minneapolis General and University of Minnesota Hospitals.

### Sister Kenny at the General

Elizabeth Kenny arrived in the United States in 1940 for a nationwide lecture tour, reporting her treatment of infantile paralysis. While in St. Paul and Minneapolis, her work met with the skepticism she had encountered previously from the medical profession. However, Doctors John Pohl, Miland Knapp, Wallace Cole, and a Minneapolis businessman, Mr. C. C. Weber, felt at least she should have a chance to demonstrate her methods. Sister Kenny (the title referring to her rank as a nurse in the Australian Army) began a series of lectures at Minneapolis General and University of Minnesota Hospitals in early 1940. In June of that year, an observation ward was opened to her at General, Station K. One year later, she was supervising wards both at General and the University and she was given the title of Guest Instructor.

Support for the Kenny treatment waxed and waned within the medical profession. She, herself, would defend her theories to the most prominent of medical authorities, very often with scathing remarks about physicians. Nevertheless, her popularity and fame grew astronomically across the United States and throughout the world as continued reports of the "miracles" of the Kenny method spread. The city of Minneapolis gave her the Lymanhurst facilities in 1942, as the Elizabeth Kenny Institute was established. Other Kenny Centers opened across the country with the polio epidemics of the late 1940s and early 1950s precipitating their need.

Her fame was so well established that when the support of the National Foundation for Infantile Paralysis was withdrawn from the Kenny Institute, in 1945, she launched her own funding drive with actor Bing Crosby as the chairman. This was also the year



Information desk in main building, 1916.



the Institute became independent of the General. In 1946, a film on her life was released starring Rosalind Russell. Sister Kenny was often photographed with famous personalities and she lunched privately with President Roosevelt on several occasions. Throughout her ten year stay in the United States, her base continued to be Minneapolis.

Despite the medical controversy she aroused, evidently her methods of treatment eased the sufferings of thousands of children. In 1952, the year of her death, Sister Kenny was voted the most important woman in America by the Gallop Poll.<sup>21</sup> Station K at Minneapolis General Hospital gave her that chance.

### Chief of Service Minutes (1937-1963) Read Like a History of Modern Medicine

Reading through the Chief of Service Minutes of 1937-63, one sees the tremendous advances in medicine unfold and also gets a glimpse of the color of the times:

- 1937 — Staff viewing of the “private preview of the motion picture ‘The Birth of a Baby’.”<sup>22</sup>  
“The question of a birth control clinic came up for discussion and was unanimously opposed.”<sup>23</sup>  
Addition and recommendation for purchase of new equipment: i.e. a new “gas machine”, an infant size bronchoscope and water vaporizer, the hospital’s first EEG equipment, a new “dictaphone in the operating room” for surgical case summaries.
- 1938 — Suggestion made that the metric system replace the apothecary in writing prescriptions.  
A Cathartic list was to be made and posted on the ward each morning “to include only the names of persons who had not had bowel movements for 48 hours.”<sup>24</sup>
- 1940 — “There was some question of whether interns should have to take blood for blood chemistry.”<sup>25</sup>
- 1941-45 Discussion of shortages during the war years: Staff, rubber goods, Xray film, drugs, and certain medical equipment.
- 1944 — Penicillin could be ordered for a patient only by the Chief of Staff.

Part II of “The General” will appear in the February, 1980 issue of Minnesota Medicine.

References will be listed at the end of Part II.



The Guardian Angel constantly watching over the hospital.

- 1947 — Ever present parking problems were brought to the attention of the hospital’s Board Chairman, the Mayor Hubert H. Humphrey.
- 1950 — Recommendation for a trial of “concentrated dextrose to make both 5 and 10 per cent solutions.”<sup>26</sup>
- 1951 — Suggestion for a trial of oral cortisone (although it was presently “unavailable”).

With the dawn of the age of the “A” bomb, the staff viewed two films in December of 1952: “Biological Warfare” and “Atomic Alerts”. The following year a motion was passed that “the use of abbreviations be eliminated in physicals, progress notes, and histories.”<sup>27</sup>

The notes end in the early 1960s with the recommendation that the State Legislature transfer the operations of the hospital from the city to the county.

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# Review

## Respiratory Tract *Aspergillus* Clinical Significance

C. VAUGHN STRIMLAN, M.D.;\* DAVID E. DINES, M.D.;\* ROSEMARY F. RODGERS-SULLIVAN, M.D.;\*  
GLENN D. ROBERTS, PH.D.;\* and WILLIAM C. SHEEHAN, M.D.\*

*Aspergillus* organisms were cultured from sputum, bronchial washings, or lung tissue of 169 patients during a one-year period. Seventeen (10%) of the patients had pulmonary disease due to *Aspergillus*, and 152 patients (90%) were considered to have "colonization" by the organism without evidence of significant disease. Of the 17 patients with aspergillosis, six had invasive aspergillosis, five had aspergillomas, four had allergic bronchopulmonary aspergillosis, and two had pulmonary infiltrates with eosinophilia. Our review indicates that cultures of *Aspergillus* from the respiratory tract alone are not sufficient for the diagnosis of aspergillosis and that most patients with positive *Aspergillus* cultures have insignificant respiratory tract contamination or colonization.

FUNGAL SPORES of *Aspergillus* are widely distributed in nature. Approximately 200 species of *Aspergillus* have been identified, and they can grow on a wide variety of substrates under a number of environmental conditions.

Any species of *Aspergillus* may infect man, but *A. fumigatus* and *A. niger* are particularly likely to grow in the respiratory tract.<sup>1</sup> Because aspergilli are frequently cultured from the respiratory tract, their clinical significance is often difficult to interpret. Usually, the organisms are not pathogenic in healthy persons, but they may become significant pathogens in invasive aspergillosis,<sup>2</sup> mycetomas,<sup>3</sup> allergic bronchopulmonary aspergillosis,<sup>4</sup> or pulmonary infiltrates with eosinophilia.<sup>5</sup> However, a positive *Aspergillus* culture may indicate pulmonary contamination or "colonization" only, without clinical evidence of significant disease, so that isolation from respiratory secretions alone is not sufficient for a diagnosis of aspergillosis.

We studied the importance of *Aspergillus* cultured from the tracheobronchial tree and its possible relationship to various respiratory disorders.

### Material and Methods

A review of the medical records of 169 patients with at least one positive sputum, bronchial washing, or lung tissue culture for *Aspergillus* was carried out at the Mayo Clinic during a one-year period from January 1,

1974, through Dec. 31, 1974. The ages of the 169 patients (109 men and 60 women) ranged from seven to 77 years, with an average of 55 years. The patients represented a predominantly Midwestern population, with variable occupations and allergic histories. Approximately 25% of the patients were cigarette smokers.

Identification and isolation of *Aspergillus* organisms were performed in the mycology laboratory in the

TABLE 1  
Disease Associated With Positive *Aspergillus* Cultures

Disease	No. of patients
<b>Aspergillosis</b>	<b>17 (10%)</b>
Invasive aspergillosis	6
Aspergilloma	5
Bronchopulmonary aspergillosis	4
Pulmonary infiltrates with eosinophilia	2
<b>Colonization</b>	<b>152 (90%)</b>
COPD* (27 no steroids; 3 with steroids)	30
Bronchial asthma, with steroids	24
Bronchial asthma, no steroids	17
Lung cancer	17
Bronchiectasis	15
Lymphoproliferative diseases (6 lymphoma; 5 leukemia)	11
Chronic cough	9
Interstitial pneumonitis (fibrosis)	5
Old tuberculous granulomatous disease	5
Active pulmonary tuberculosis	2
Active pulmonary histoplasmosis	2
Radiation fibrosis	2
Others†	13

\*COPD = chronic obstructive pulmonary disease.

†Others, one each: atypical mycobacterial infections, pulmonary sarcoidosis, right middle lobe syndrome, pneumococcal pneumonia, acute tracheobronchitis (?viral), postpneumonectomy (with empyema), polyarteritis nodosa, kyphoscoliosis (with cor pulmonale), pulmonary embolism (with left upper lobe infarction), chronic sinusitis, chronic granulomatous disease of childhood (pulmonary fibrosis), primary amyloidosis, and old left fibrothorax (secondary to congestive heart failure and pleural effusion).

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Read at the meeting of the American Thoracic Society, San Francisco, May 15 to 18, 1977.

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### Section of Clinical Microbiology.

Data on the 169 patients were gathered regarding the primary pulmonary diagnosis, associated clinical diagnosis, symptoms, physical findings, results of routine blood tests and urinalysis, *Aspergillus* immunodiffusion test results, skin tests against *Aspergillus* extracts, cultures for *Aspergillus*, chest roentgenographic observations, diagnostic studies, treatment, and follow-up.

Based on the clinical, laboratory, roentgenographic, and mycologic findings, the patients were classified as having pulmonary disease due to *Aspergillus*, that is, invasive aspergillosis, aspergillomas, allergic bronchopulmonary aspergillosis, and pulmonary infiltrates with eosinophilia, or as having insignificant colonization with *Aspergillus*.

### Results

Seventeen patients (10%) had significant respiratory disease due to *Aspergillus*. Of the 17 patients, six had invasive aspergillosis, five had aspergillomas, four had allergic bronchopulmonary aspergillosis, and two had eosinophilic pneumonia with *Aspergillus* in the sputum. The remaining 152 patients (90%) had insignificant respiratory tract "colonization" by *Aspergillus* species, without evidence of significant disease (Table 1).

A total of 621 fungal cultures were obtained from the 169 patients (approximately four cultures per patient), and of these, there were 255 positive cultures for *Aspergillus* (Table 1). The most productive culture sites were spontaneous and induced sputa, bronchial washings, and lung tissue, which accounted for 248 of the 255 positive cultures (97%). Seven other positive cultures (3%) were obtained from gastric washings, mucus plugs, or transtracheal aspirations. No positive *Aspergillus* cultures were obtained from blood or urine specimens in this series.

Although various aspergilli were cultured, the most common species were *A. fumigatus* and *A. niger* (92%) (234/255). Other species included *A. flavus*, *A. versicolor*, *A. glaucus*, and *A. terreus* (8%) (21/255).

Immunodiffusion tests using antigens of *A. fumigatus* and *A. niger* were performed on 81 of the 169 patients. Of the 81 patients, 12 (15%) had positive reactions, including four with allergic bronchopulmonary aspergillosis, three with invasive aspergillosis, three with mycetomas, one with bronchial asthma, and one with chronic granulomatous disease of childhood and pulmonary fibrosis.

Skin tests against *Aspergillus* extracts were done in 74 of the 169 patients. Of the 74 patients, 19 (26%) had

positive immediate skin reactions, including four with allergic bronchopulmonary aspergillosis, two with invasive aspergillosis, one with an aspergilloma, seven with asthma, and five with miscellaneous respiratory disorders.

### Discussion

Inhalation of aspergilli may lead to various clinically significant bronchopulmonary diseases<sup>6-8</sup> (Table 2).

In our series, four patients had bronchopulmonary aspergillosis; all were asthmatic. Bronchopulmonary aspergillosis in our patients with bronchial asthma was characterized by migratory, transient lung infiltrations, low-grade fever, peripheral blood and sputum eosinophilia, expectoration of mucus plugs, periodic wheezing, and a positive *Aspergillus* sputum culture. Patients had a positive serologic test for *Aspergillus*, a positive immediate skin test to *Aspergillus*, and an

TABLE 2

#### Classification of Pulmonary Aspergillosis

- A. Noninvasive pulmonary aspergillosis
  1. Allergic bronchopulmonary aspergillosis
  2. Aspergilloma
  3. Pulmonary infiltrates with eosinophilia
  4. Hypersensitivity pneumonitis
- B. Invasive pulmonary aspergillosis
  1. Associated with altered host defenses secondary to:
    - a. Malignant disease
    - b. Immunosuppressive therapy
- C. Colonization

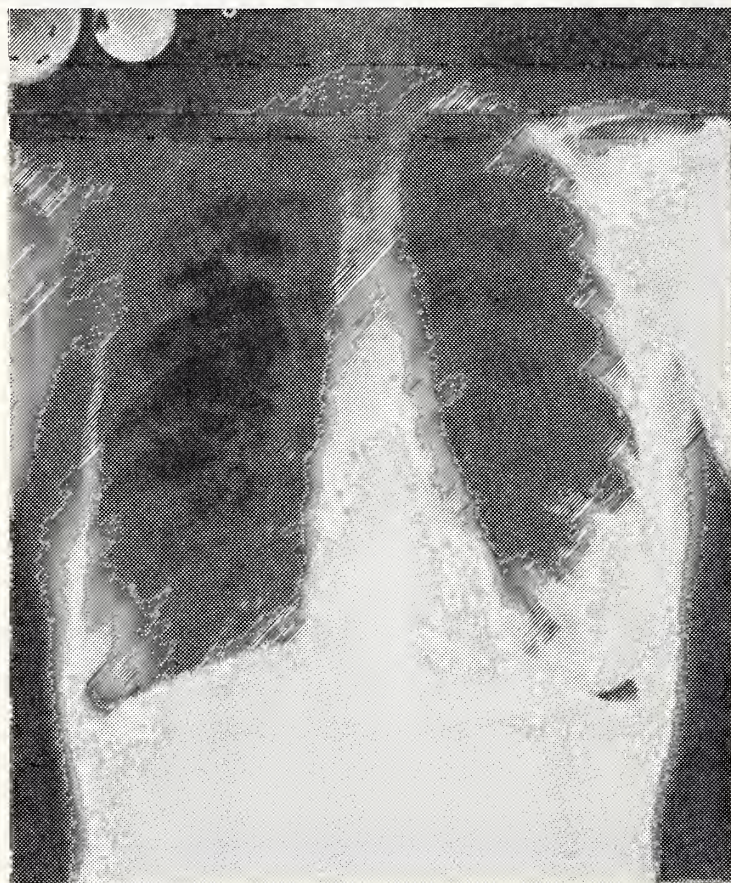


Fig. 1 — Chest roentgenogram demonstrates nodular infiltrates of bronchopulmonary aspergillosis in upper lobes of both lungs.



elevated IgE level. All four patients had an elevated IgE level that varied from 2,360 to 3,080 ng/ml. Pulmonary function studies showed an obstructive ventilatory pattern. The chest roentgenogram (Figure 1) characteristically showed migratory pneumonitis. The prognosis was relatively good with steroid therapy and treatment of the underlying asthma.<sup>9</sup> Bronchiectasis was not seen in any of our four patients with bronchopulmonary aspergillosis.

Five of our patients had aspergillomas; all five had positive sputum cultures. Three of the five had positive serologic reactions, but only one had a positive immediate skin reaction. Aspergilloma, a "fungus ball" lying in a thin-walled cavity of the lung, usually occurred in the upper lobes (Fig. 2 (A) and (B)) or in the superior segments of the lower lobes. The mycetoma was usually unilateral and developed at the site of previous pulmonary diseases (saccular bronchiectasis, tuberculous cavities, and fungal infections). Mycetomas are usually asymptomatic, but massive hemorrhage may be a complication. Medical therapy is of little value because amphotericin B, nystatin, and 5-fluorocytosine do not penetrate the cavity wall and the fungal mass. Although approximately 10% of mycetomas undergo spontaneous lysis and resolution, the treatment of choice is surgical resection, usually lobectomy.<sup>10</sup> Two of our patients had curative resections. Operative complications include empyema and bronchopleural fistula. The long-term prognosis<sup>3,11,12</sup> depends on the underlying lung disease and the preoperative pulmonary function status of the patient.

Six of our patients had invasive aspergillosis. All six had a lymphoproliferative disorder and were receiving immunosuppressive or corticosteroid therapy or both. Serologic tests were positive in three of the four patients who were tested, and the immediate skin test was positive in two patients tested. Roentgenograms of the chest showed diffuse alveolar infiltrates (Figure 3). Three patients were successfully treated by surgical resection and amphotericin B. Medical therapy with amphotericin B alone or in combination with rifampin has been efficacious.<sup>13,14</sup> Nevertheless, the prognosis is very poor, with a 60 to 70% mortality directly related to the *Aspergillus* infection. Because *Aspergillus* is second only to *Candida* in causing fungal infections in the altered host, a positive *Aspergillus* sputum culture should be critically evaluated in the compromised or immunosuppressed host. Aggressive diagnostic efforts are urgently indicated in such a predisposed patient with lung infiltrates of unknown cause.

In our series, one patient had pulmonary infiltrates

with eosinophilia and another had pulmonary infiltrates with eosinophilic pneumonia. The pulmonary infiltrates were characteristically migratory and usually were associated with peripheral blood eosinophilia. The patients had a mild cough or no respiratory symptoms. Fever was absent. Roentgenographically, the infiltrations were of a pneumonic type, with a tendency to migrate from one portion of the lung



Fig. 2 — (A) Chest roentgenogram shows "fungus ball" in left upper lobe cavity.

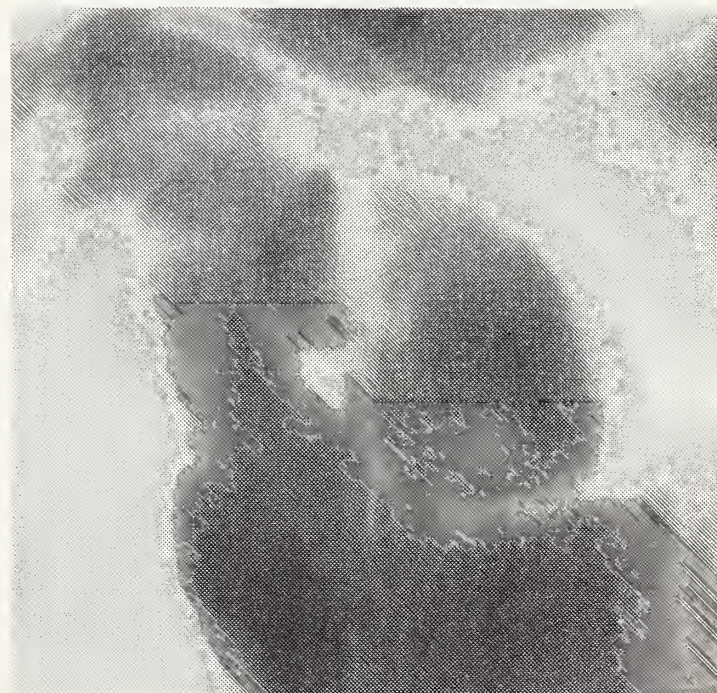


Fig. 2 — (B) Tomogram showing fungus ball in cavity.



to another, and they were seen as peripheral densities adjacent to the pleura, with clear zones centrally (Figure 4). The diagnosis is usually inferred from the clinical presentation. The immunodiffusion test for



Fig. 3 — Invasive aspergillosis. Demonstrating diffuse right upper lobe alveolar infiltrate.

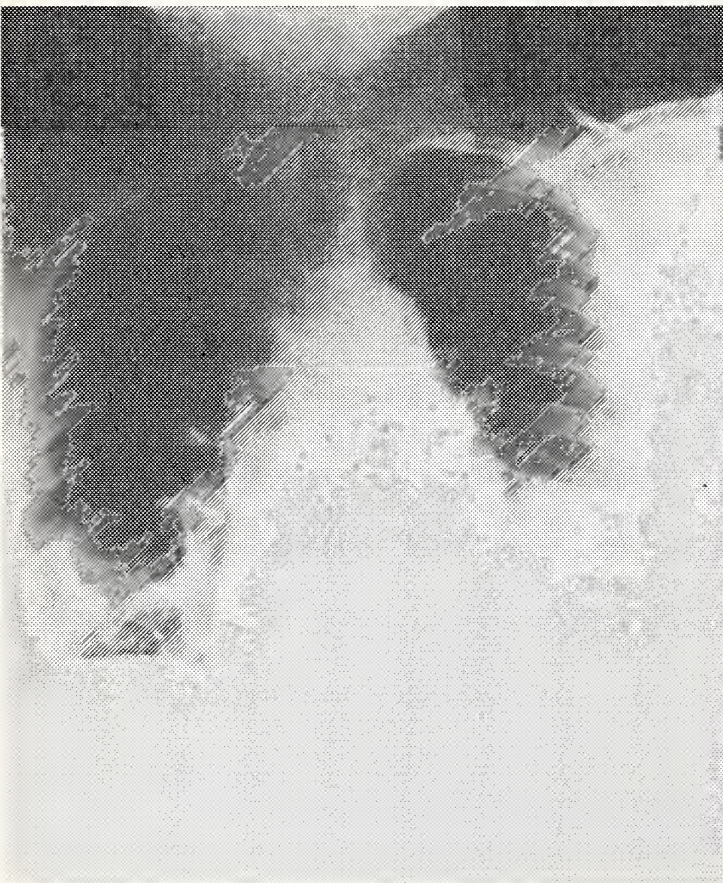


Fig. 4 — Chest roentgenogram demonstrates alveolar infiltrate involving left lower lung field in patient with pulmonary infiltrates with eosinophilia.

*Aspergillus* and the skin test may be negative. The disease may be self-limited. When asthma is associated with pulmonary infiltrates with eosinophilia, the patient is usually more symptomatic. Treatment is with corticosteroids, and the response is usually good. However, the disease may recur after discontinuance of treatment, sometimes in the same locus in the lung.<sup>5,15</sup> Both patients had clearing with corticosteroids, and the sputum became negative. We do not know the significance of the two positive sputa for *Aspergillus* found in our two patients with pulmonary infiltrates with eosinophilia.

Extrinsic allergic alveolitis or hypersensitivity pneumonitis secondary to the inhalations of *A. clavatus* has been noted in malt workers. This is attributed to a type III IgG-mediated hypersensitivity reaction.<sup>16</sup> No patients in our series had extrinsic allergic alveolitis secondary to *Aspergillus*.

The diagnosis of significant pulmonary *Aspergillus* infections is difficult. The diagnostic workup should include a chest roentgenogram, multiple sputum or bronchial washing cultures, immunodiffusion test, skin tests against *Aspergillus* extracts, IgE determination, blood eosinophil count, sputum for eosinophils, pulmonary function studies, and bronchograms, if indicated. Lung biopsy may be necessary for definitive diagnosis. Laboratory studies should be correlated with the clinical findings. The differentiation of patients with bronchopulmonary aspergillosis from asthmatic patients remains a difficult clinical problem. It has been reported that 13 to 38% of asthmatic patients have positive immediate skin reactivity to *A. fumigatus*.<sup>8</sup> The incidence of serum-precipitating antibodies against *A. fumigatus* has been reported to be 3% in nonallergic asthmatic patients, 25% in allergic asthmatic patients, and 69 to 90% in patients with bronchopulmonary aspergillosis.<sup>17,18</sup>

*Aspergillus* organisms are prevalent, and any species may infect man. Approximately 16% of normal persons may have *Aspergillus* cultured from sputum samples.<sup>19</sup> Culture from the sputum alone cannot be taken as proof of a diagnosis of pulmonary aspergillosis.

In a 1959 study, Pepys and associates<sup>1</sup> obtained sputum cultures for *Aspergillus* from 2,080 patients with chest disorders. Of the 2,080 patients, 168 (8.1%) had positive sputum cultures. Only 25 of the 168 patients (15%) had clinically significant chest problems related to *Aspergillus*, including 17 with allergic bronchopulmonary aspergillosis, four with aspergillomas, and four with pulmonary infiltrates with eosinophilia. The remaining 143 patients (85%) had



*Aspergillus* organisms in the tracheobronchial tree, which represented "colonization," and they had no evidence of clinical illness or tissue invasion. Pepys and associates<sup>1</sup> concluded that isolation of *Aspergillus* from the sputum alone is not sufficient for the diagnosis of aspergillosis. In the present study of 169 patients, only 10% of patients with *Aspergillus* cultured from a pulmonary source had clinically significant pulmonary disease, such as allergic bronchopulmonary aspergillosis, aspergilloma, invasive

aspergillosis, or eosinophilic pneumonia. The remaining 90% of patients had a positive sputum culture without clinical evidence of significant pulmonary disease even after adequate follow-up. Aspergillosis cannot be diagnosed on the basis of cultures of *Aspergillus* from the respiratory tract alone. Most patients have positive *Aspergillus* cultures that indicate only insignificant respiratory tract contamination or colonization.

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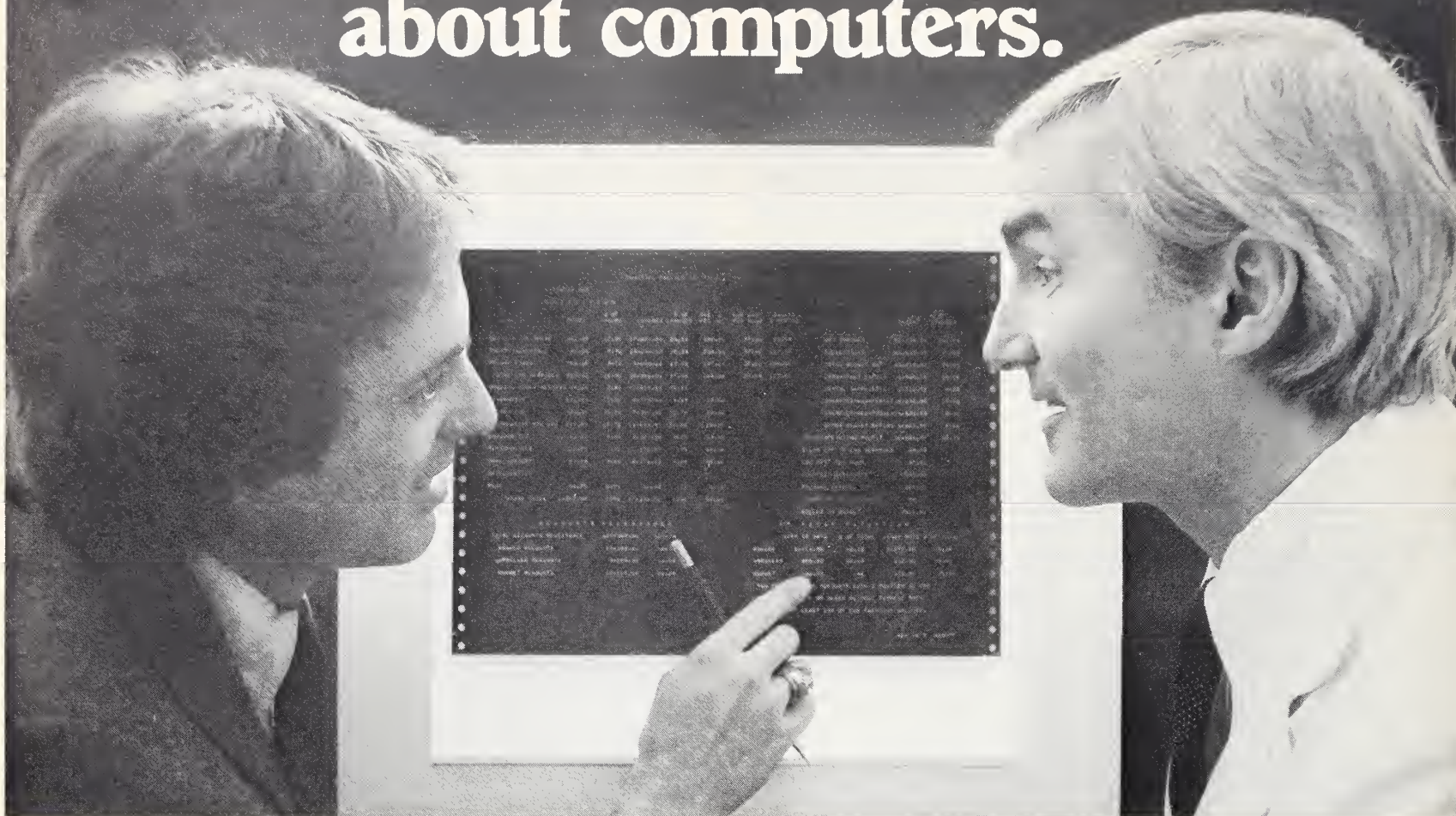
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# Special Article

## Body Image, Personality, and Life Event Changes after Jejunoileal Bypass Surgery for Massive Obesity

GLORIA R. LEON, PH.D.\*, ELKA D. ECKERT, M.D.†, DONALD TEED, B.A.‡, RICHARD L. VARCO, M.D.#, and HENRY BUCHWALD, M.D.§

A group of 24 massively obese persons (predominantly women) were studied six months prior to jejunoileal bypass surgery and again in-hospital awaiting surgery. A second group of 48 persons were followed from the in-hospital period prior to surgery, and then 3 months, 6 months, and one year post-surgery. There was an increasing improvement as weight loss progressed in aspects of body image, personality, and self-attitude evaluation. Concomitant with weight loss, a decline was evident in anxiety and depression. A general improvement in mood also was demonstrated for the group as a whole. Eating patterns did not change for the majority of persons. Eight individuals who did not respond to the follow-up questionnaires indicated that they were experiencing marked psychological or physical problems. In general, however, the persons in the study indicated satisfaction with the life changes and body state changes that occurred after jejunoileal bypass surgery.

**J**EJUNOILEAL BYPASS surgery for massive obesity has generated considerable interest due to the findings of significant weight loss over time, ranging from 35% average weight loss<sup>1</sup> to 39%<sup>2</sup>. Since the greatest amount of weight loss tends to occur in the first year after surgery, many persons experience a dramatic change in their physical appearance in a relatively short period of time. This change to a more normal weight status may have important psychological significance because the majority of persons undergoing bypass surgery have been obese and therefore of deviant body state since childhood.<sup>3,4</sup>

The present study was designed to evaluate the psychological, body image, and interpersonal concomitants of bypass surgery. Information about important life changes subsequent to the operation also was obtained. A further purpose was to monitor the changes in eating patterns, physical symptoms, and medications prescribed after surgery. The specification of psychological and social functioning prior to surgery was considered crucial in evaluating the changes occurring after surgery.

### Methods

#### *Subjects*

The persons participating in this study were referred to, or had come voluntarily to, one of the investigators (H.B.) at the University of Minnesota Hospitals requesting intestinal bypass surgery for massive obesity. All of the persons were at least 100 pounds above ideal body weight, had been unsuccessful with a variety of other methods of weight reduction, and were judged through psychiatric screening (E.D.E.) to be competent to adhere, when this was questioned, to the necessary medical regimen for an indefinite period of time after surgery.

Group 1 consisted of 24 persons (20 females and four males) who were evaluated for the first time at least six months prior to surgery. The age of the females ranged from 18 to 60 years; the median age was 36.25 years. For the males, the age range was from 28 to 40 years; the median was 28.75 years. The median weight of the females was 251.80 lbs. (ranging from 220 to 377 lbs.). The median weight of the males was 338.50 lbs. (ranging from 322 to 355 lbs.). Juvenile onset of obesity was reported by 85.0% of the persons in this group. In-hospital information was obtained on 16 persons (14 females and two males): 67%.

Group 2 consisted of 48 individuals (42 females and six males) who were evaluated for the first time after

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admission to the hospital several days prior to surgery. The age range of the females was from 21 to 53 years; the median was 33.0. For the males, the age range was from 24-35 years; the median was 27.5 years. The median weight of the females was 267.0 lbs. (ranging from 220 to 375 lbs.). The median weight of the males was 366.0 lbs. (ranging from 275 to 400 lbs.). Juvenile onset of obesity was reported by 82.2% of the persons in this group.

Follow-up cooperation was obtained for 35 persons (31 females and four males): 73%. The mean one year weight loss was 93.83 lbs. (ranging from 50-190 lbs.).

The persons in both groups were white, of varying socio-economic status.

#### *Measures*

The MMPI, SCL-90 mood scale, Self-Attitude Questionnaire, Personality and Body Image Semantic Differential, and Psychiatric History Questionnaire were administered. A detailed eating pattern questionnaire was constructed for this investigation, as well as check list forms for monitoring physical symptoms and the use of medications.

#### *Procedure*

Group 1 was evaluated at least six months prior to surgery, after the persons had been accepted for jejunoileal bypass surgery and placed on a waiting list. The second test period occurred several days before surgery when the person had already been admitted to the hospital.

The patients in Group 2 were evaluated for the first time in-hospital several days prior to surgery. They were administered the same tests given to the patients in Group 1. Follow-up evaluations using the various test measures were carried out three months, six months, and one year after surgery.

### **Results**

The strategy of evaluating two groups of persons undergoing intestinal bypass surgery was to use the Group 1 data six months prior to surgery as a baseline measure and for comparison to the data obtained when the person was hospitalized prior to surgery. Otherwise, the prospect of surgery and possible uncertainty about personal outcome could have been confounding factors in interpreting the results obtained at the in-hospital time period.

The results indicated that Groups 1 and 2 responded in a quite comparable manner on all measures except the MMPI at the in-hospital period, and the few significant differences could have occurred by chance. The differences in mean MMPI profiles for Group 1

and Group 2 point to the lack of any consistent psychological pattern of emotional make-up in persons who are massively obese. The profiles were all within normal limits.

A comparison of the MMPI results for Group 1 six months prior to surgery and at the in-hospital period demonstrated a significant decline in the following scales: Hypochondriasis, Hysteria, Psychopathic Deviate, Psychasthenia, Schizophrenia, and Social Isolation. Scale increases were found on Femininity and Ego-Strength. These results point to a significantly lesser degree of bodily concerns, impulsivity and interpersonal tensions, anxiety, social isolation, and introversion in-hospital as compared to the prior six month period.

Matched t-tests in Group 2 females were performed comparing the scores obtained on the MMPI at the in-hospital assessment and the one year follow-up period. The mean scores for all of the scales were within the normal range. Significant scale reductions were found one year post-surgery on the Depression and Social Introversion Scales ( $p = 0.01$ ), and a significant increase occurred on the Ego-Strength scale ( $p = 0.04$ ). These results therefore indicate an improvement in mood, ego strength, and activity level, and a decline in social isolation one year after surgery. All of the T-score means for the scales were within the normal range.

The analysis of the SCL-90 mood scale indicated significant reductions in scale elevation on the somatization, obsessive-compulsive, interpersonal sensitivity, and anxiety scales ( $p < 0.01$ ). The significant linear trend component indicated a progressive decline in these scales concomitant with weight loss.

Analysis of variance for repeated measures were performed on the body and personality judgments in-hospital, and at the three month, six month, and one year follow-ups. All but three of the judgments for "My Body Right Now" showed highly significant differences over time ( $p < 0.001$ ). The ratings that showed significant changes all shifted toward a more favorable body image. The ratings for the concept "My Personality Right Now" exhibited significant changes over time on nine of the sixteen scales. In all cases, the change was in the positive direction. Over time, the persons rated their personalities as more attractive, outgoing, self-assured, quick, active, comfortable, popular, and powerful, and less preoccupied with weight.

The women in the study rated themselves as more physically attractive, thinner, more feminine (physi-



cally), more sexually attractive, more in control of and pleased with their eating patterns, and more sociable. There was no significant change reported in sexual activity or sexual pleasure.

The post-surgery psychiatric history of the group was assessed. At three months and six months, 97.1% indicated that they had not been treated by a psychiatrist. The item was left blank by 2.9%. At the one year follow-up, 11.4% indicated that they had sought some type of psychiatric treatment, while 88.6% indicated that they had not. There were no hospitalizations for psychiatric reasons reported for the group.

Evaluation of the number of physical symptoms indicated by the patients at each evaluation period showed no significant change in number over the one year follow-up period (a range of 5.38 — 6.62 symptoms). However, there was a change in the proportion of specific symptoms reported. Over the one year period, there was a decrease in reports of tiredness, lack of energy, backache, and swollen legs and ankles. Some persons reported increased appetite followed by decreased appetite at one year, while others reported the opposite trend. There was an increase up to the six month period in reports of rectal pain and diarrhea and then a decrease by the one year follow-up. An increase over time was noted in reports of hair loss and smelly bowel movements. At all four evaluation periods, approximately 45% of the patients indicated that they did not consider these symptoms a problem.

The number of reported daily bowel movements ranged from a mean of 1.41 per day in-hospital, 2.41 at the 3 month follow-up, 2.21 at the six month, and 2.18 at the one year follow-up period. The number of medications taken per day ranged from a mean of 0.77 in-hospital, 4.74 at three months, 3.77 at 6 months, and 3.03 at the one year follow-up. Over the one year period, there was a decrease in the use of tranquilizers, an increase followed by a decrease after the six month period in reported use of potassium, calcium, lomotil, and multi-vitamins, and an increase in the use of vitamin B<sub>12</sub>.

The Eating Survey Questionnaire did not show any significant changes over time in eating patterns for the group as a whole. However, there was a trend toward a decrease in the amount of food eaten at the evening meal ( $p = 0.071$ ).

#### *Non-Responder Information*

The 13 persons in Group 2 who did not return the follow-up materials were contacted by phone several

times at each evaluation period. They generally indicated that they did not want to be bothered with filling out the questionnaire materials. Five of these persons reported that they were pleased with their weight loss and felt much happier after the operation. Four persons reported that they were having extremely severe physical problems subsequent to surgery, and two of this group indicated severe psychological problems as well. Four other persons reported severe psychological or family problems ranging from anxiety or insomnia to home difficulties because of their engaging in sexual relationships with many partners. Thus, the inclusion of the non-responder group indicates that 12.5% of the total sample ( $N = 6$ ) reported severe psychological problems and 16.6% of the total sample ( $N = 8$ ) reported either severe psychological or physical difficulties, or a combination of these problems subsequent to bypass surgery.

#### **Discussion**

The results of this study indicate that for this particular group of massively obese persons, i.e., those without significant psychological deviance, jejunoileal bypass surgery had markedly beneficial psychological effects for the majority of persons. The information on body image obtained from a variety of measures demonstrated a clear change to an increasingly more favorable self-evaluation of body and personality as weight loss progressed.

The MMPI findings in the present study further substantiated a significant reduction in dysphoric mood, an increase in activity level, and a decline in social introversion with weight loss. A decline was evident in physical concerns, anxiety, interpersonal frictions, social isolation, and withdrawal when persons were already in the hospital and involved in the process of preparing for the surgery that was to take place in the next few days. These findings suggest that these massively obese individuals were facing surgery with a positive mood and attitude about the changes that would occur after the operation. However, changes in attitude about one's body and personality were not evident during the pre-surgical waiting period nor in the hospital prior to surgery. These changes were clearly demonstrated in the follow-up period though, as weight loss progressed subsequent to surgery.

A note of caution is in order in terms of the implications of this study. It seems reasonably clear that there was a marked enhancement of psychological functioning after jejunoileal bypass surgery for the majority of persons in this investigation. However, some persons from the non-responder group were



experiencing psychological and physical problems. Other persons required psychological or psychiatric intervention to deal with the changes in their lives produced by the marked modification in body state. Therefore, it seems appropriate to have services

available for those persons who need some form of counselling to cope with the various changes in their lives as part of a comprehensive follow-up care program for all massively obese individuals treated by surgical means.

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#### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

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4. Has had a relatively long experience in the field of medical science or a related field.

Nominations for the May 1980 awards should be sent immediately to:

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Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.

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#### Cover Painting "Spring Dream"

Dr. Robert O. Fisch painted the cover oil painting in the winter of 1979. His subject was the spring tulips of the Como Park Observatory. This is an artistic escape from the harsh Minnesotan winter to the desire for Spring and flowers.

Dr. Fisch is a Professor in the Department of Pediatrics, University of Minnesota Medical School. He considers painting not as a hobby but an ultimate experience in creativity. He will have a painting exhibit from January 3-17, 1980 at the Coffman Gallery 1, Minneapolis.



# Editorial

## Complications of Cancer Therapy

THE ARTICLE on "Liver Injury Secondary to Radiation Therapy for Breast Cancer" in the November issue,\* raises some very interesting points. It has been very well known that various agents used in the treatment of cancer to produce side effects and complications. These run the gamut from surgery, radiation, chemotherapeutic, hormonal agents, etc. No agent if used injudiciously is free from injurious side effects.

Radiation is one agent that has been implicated in a number of situations as a complicating factor when in fact this has not been so. It therefore behooves the reader when evaluating articles that implicate radiation as a complicating agent to be certain that indeed radiation was a causative agent in the production of the complication. The problem may be due to other factors, and if these are overlooked, possible treatment for the problem may not be instituted or the presence of other diseases, may not be discovered.

Unfortunately, in the present case report, we are not given the treatment technique used to treat the chest wall. In most institutions chest wall irradiation is delivered through tangential ports which, in most instances, do not expose the liver to any irradiation. In the approximately 100 cases treated in the last ten years here at the University of Minnesota with tangential chest wall radiation there have been no instances of

liver damage secondary to the radiation. In addition, this has not been reported in the literature, to my knowledge. This is not meant to imply that liver damage cannot develop with direct radiation to the liver. Indeed it does, and indeed the doses mentioned by the author in the article are capable of producing radiation damage if delivered directly to the liver.

It is only fair to note that the possibility exists that the liver damage was not due to the radiation and indeed may have been caused by chemotherapy. The chemotherapeutic agents used in this patient are associated with a high incidence of complications of varying degrees of severity. Friedman and Carter<sup>1</sup> report that hepatotoxicity has been reported with the administration of methotrexate. This has also been reported in other publications.<sup>2</sup> Cyclophosphamide has also been reported to produce hepatic damage.<sup>2</sup>

In summary, it is important to be aware of the possibilities of complications secondary to treatment in the use of any modality. Although it is possible that radiation did produce damage described in the article, it is also possible that chemotherapy alone or in combination with the radiation produced damage. It is important for the physician to be aware that complications do exist and that careful monitoring and careful application of any treatment is essential to produce the best results and the fewest complications.

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\*Hoffman, Neil R.: Liver Injury Secondary to Radiation Therapy for Breast Cancer. *Minnesota Medicine* 62:11:778, 1979.

†Professor and Head, Department of Therapeutic Radiology, University of Minnesota Medical School, Minneapolis.

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## Ultrasound of Renal Transplant Complications with C.T.

THE ARTICLE in this issue on "Ultrasound of Renal Transplant Complications" illustrates perfectly the application of a noninvasive technique to differentiate pathologic conditions that present similarly, but that require different treatments. Its usefulness as an aid to diagnosis of fluid collections or other pathology is clear, and further comment is hardly needed.

What is worthy of comment in the article by Scholl and Feinberg\* is the statement that opens their article: "Renal transplantation. . . has been responsible for the stimulation and development of a great volume of basic and practical immunologic knowledge." This statement has implications beyond those probably intended by the authors; indeed, the spinoffs from organ transplantation over the past several years have led to advances and stimulation of nonimmunological fields as well, only one of which is illustrated by the article. For example, tissue typing began as an adjunct to transplantation. The discovery that certain diseases are associated with particular HLA antigens has resulted in a new tool for the study of the genetic aspects of disease. Tissue typing is also used in forensic medicine and even anthropology.

Another example is in the understanding of the

pathology of the complications associated with diabetes. The fact that diabetic nephropathy develops in kidneys taken from nondiabetic donors after transplantation to diabetic recipients is one of the strongest bits of evidence that the microvascular complications associated with diabetes are truly secondary to the metabolic defect, and not an independent, genetically determined manifestation of diabetes. This knowledge in turn, provides an impetus to provide good metabolic control to diabetic patients in an attempt to prevent or halt the progression of the associated complications.

Other examples could be given if space permitted. Multiple medical specialties are involved in the management of transplant patients. Complex problems arise in these patients — some of which are illustrated in the article by Scholl and Feinberg. Their article provides an example of the challenge such patients provide to a medical specialty — radiology, in this instance. The interaction of transplantation with practically every aspect of medicine is a process that should continue to provide benefits beyond those that are immediately applicable to the patient with renal failure.

\*See page 11.

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# Indo-Chinese Refugees

## Medical Care of Southeast Asians — Compliance

R. B. BREITENBUCHER, M.D.\*

Compliance with medical regimens is a universal problem and not unique to S.E. Asians, but S.E. Asians may present unique compliance problems. A frustrated sponsor tells of spending hours taking a S.E. Asian to a physician and having the prescriptions filled, only to have the patient come home and throw the medication down the toilet, an example of non-compliance in the extreme. Was this caused by lack of trust? Had the physician inadvertently insulted the patient by violating a cultural taboo?† Was a misunderstanding created in translation by the Interpreter? Although not readily apparent in modern practice of medicine, concepts of disease and the healing arts have been historically intermingled with religious beliefs and practices. Akin to this is a belief in the curative properties of "natural substances" and distrust for "artificial chemicals." Could something of this nature have resulted in the patient's distrust for modern medical practice? Could the patient have had a bad experience with side effects or toxicity from medication in the past? We will never know about this patient because she couldn't be persuaded to come back. It does serve to illustrate that a good deal of time and money can be spent in providing health care, only to have it all go for naught if compliance is not secured. The following discussion will deal principally with universal problems in compliance with some comments related specifically to S.E. Asians. The discussion suffers some from the writer's lack of a comprehensive knowledge of views, rooted in culture which some of these people may have about disease processes. This problem becomes more complex when it is realized that S.E. Asians are not a single cultural entity, but are people of diverse origin and beliefs.

The following are universal problems for compliance with medical regimens:

1. Trust in prescribing physician.
  - a. Thoroughness of the examination as perceived by the patient.
  - b. Amount of time spent by the physician as perceived by the patient.
  - c. Interest of the physician in the patient and patient's problems as perceived by the

patient.

- d. Attitude of the physician towards the prescribed medication or medical regimen.
2. Trust in the regimen itself.
  - a. Attitude of the patient towards medications in general.
  - b. Patient's perception of whether the regimen is reasonable.
3. Cost factor.
4. Transportation factor.
5. Ability of patient to remember the regimen.
6. Patient's understanding of the regimen.
7. Side effects or toxic effects of medications.
8. Patient's attitude towards the illness or disability.
9. Patient's concept of physiology and disease processes.

### *Trust in Prescribing Physician*

Trust in the physician and the prescribed medical regimen influences compliance. Trust is influenced by the patient's perception of the physician's thoroughness in data gathering and the examination itself. If the patient perceives that the physician has not listened or examined carefully enough, the patient may feel that the physician's conclusion, and hence the prescribed regimen, may be erroneous. Thoroughness in the physician's terms may not be interpreted as such by the patient. For example, a physician, who in pursuit of a thorough examination attempts to examine the head of a S.E. Asian without first requesting permission, may find that a rapport with the patient has been jeopardized. In some cultures, there is a taboo about having one's head touched by another. Such patients may feel insulted by finding the physician's unsolicited hands on their head. Thoroughness as perceived by the patient is not always correlated with the amount of time spent. The patient seems to place a good deal of emphasis on how attentive they feel the physician is. Patients who have chronic, incurable disease, which is not life-threatening, tend to respond better to physicians who are more attentive and treat them in a more personal way. On the other hand, patients who have potentially lethal disease, such as coronary disease, often respond more favorably to a physician who takes

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†See Olness, Karen: Minnesota Med 62:871, December, 1979.



a more impersonal, businesslike, and somewhat authoritarian approach. The attitude of the physician towards the prescribed regimen is a major factor in compliance. Regimens presented with a degree of enthusiasm and hope are more apt to be complied with than regimens which are presented with a more indifferent or even pessimistic attitude. This may present a dilemma for some physicians who are concerned about being objective and intellectually honest with their patients when presenting proposed regimens. Some of their patients may be less compliant with this approach than the approach of "this is just what you need; this will cure you."

#### *Trust in Regimen Itself*

Some patients seem to have an innate trust and even desire to take medications. They are apt to be very compulsive about any regimen which is prescribed. On the other hand, there are patients who are rather cynical about medications, distrust them, fear the consequences of toxic or side effects, would rather "trust in nature," etc. Some of the latter will be more compliant if physicians bring them into the decision-making process by carefully explaining the disease, prognosis, and therapeutic options. Patients are not apt to be compliant with regimens that seem unreasonable to them. It is important to carefully go over therapeutic regimens with patients in order to find out whether they think they can follow it, and to deal with any doubts they may have.

#### *Cost of Medication*

The cost of medications is a factor. On the one hand, if medications are very expensive, the patient has to be really convinced of its worth before complying. He or she may even try to cut down on the amount of the medication used in order to save money. On the other hand, if medication is too cheap, it may be viewed by some as too cheap to be good. In dealing with S.E. Asians, it may be advisable to have their medications paid for without the money having to go through their hands. If they have to pay the money for medications themselves, there may be a temptation to use it for something else.

#### *Transportation Factor*

It may be difficult for some patients to get transportation to clinics, adversely affecting compliance. For patients who utilize a clinic pharmacy, as most of our patients do, it is important to see to it that their prescription refills coincide with clinic visits. The transportation factor is a major one with the S.E. Asian

immigrants.

#### *Patient's Ability to Remember Regimen*

The inability of the patient to remember to take medications as prescribed is a common problem. It is not correlated with intelligence. It is particularly difficult for patients who are taking medications for asymptomatic diseases or for prophylactic reasons. It helps to make patients aware of the difficulties of compliance by discussing it with them at the time the prescription is written. They should also be encouraged to discuss compliance problems with the physician. Patients are often embarrassed to bring up such matters, thinking that the problem is a singular one for them. It is often helpful for the patient to enlist the aid of a member of the family as a compliance enforcer. It is essential to discuss exactly how the patients are to take medications and work out a regimen which is compatible with their life style. Medication should be put in a place where it can be readily observed. One method is to have a full day's supply of medication set out at the beginning of each day so the patient knows whether or not he has taken his quota. When medications cannot be put out because of small children, reminders should be placed in areas frequented by the patient. When possible, medications should be related to such naturally recurring functions, such as arising, mealtimes, and bedtime. All regimens should be kept as simple as possible. There should be a minimum number of pills and a minimum number of doses prescribed. This is particularly important for patients who are working and must be away from home during the day. Many drugs, particularly those that are used in hypertension, can be just as effectively used on a b.i.d. schedule as on a more conventional q.i.d. schedule. If a medication is to be varied on an alternate day schedule, it is much easier for the patient to remember to take a given dose on Mondays, Wednesdays and Fridays and the alternate dose on the other days of the week. For drugs such as Coumadin or Digoxin, such regimens are equally as effective as one given on alternate days. Patients have trouble remembering what they took the day before, and marking things on a calendar is a bother for most of us. If it is important that the drug be taken on alternate days, as with steroid regimens, the patient should be instructed to take the dose on odd number days of the month and omit them on even numbered days (which will have to be changed, depending upon whether the months have an odd or even number of days). When prescribing estrogens cyclically, having the patient take the medication for the first 21 days of each month



eliminates calendar marking. Patients who are on prolonged regimens which are prophylactic or for asymptomatic diseases should be seen periodically. In this way, the physician demonstrates to the patient that the regimen is important enough to deserve his attention and gives him an opportunity to reinforce the regimen. A patient may be more apt to comply if told the reasons for the length of treatment prescribed, frequency of dosage, and importance in terms of what the treatment is designed to do. Physiological and pharmacological explanations can usually be made in terms that the patient can understand without becoming too simplistic. Sometimes patients, who are told only that they are taking a "thyroid pill," may get the impression that the pill is designed to treat the thyroid, and stop the medication when they begin to feel better.

#### *Patient's Understanding of Regimen*

Confusion and misunderstanding about medication instructions is a major problem. The physician cannot be too explicit about instructions as to exactly how medications are to be taken, the exact relationship to other medications, exactly what time, etc. Again, the program has to be compatible with the patient's lifestyle. It has been repeatedly shown that instruction to take medications q.i.d., q 12 H, q 8 H, etc., most of the time leads to a wide variety of interpretation by patients and to compliance which is not intended by the prescribing physician. When a regimen is particularly complicated, it is useful to sit down with the patient and write out exactly when he/she is to take each of the various medications. A patient can feel very hopeless about compliance when he/she goes to the drug store with a handful of prescriptions and comes back with a bag full of bottles with varying instructions on the labels. It is better that the patient has a sort of a roadmap written out to guide him through the morass of medications. When several medications are being prescribed, it is often helpful to choose brands of medications which are different in size, color, or shape so that the patient does not end up with several prescriptions all of which are little white pills.

#### *Side Effects or Toxic Effects of Medications*

The patient must know about the possibility of serious side effects or toxic effects of medications. This can be overdone. If one were to read all of the possible effects that may derive from a given drug, very few patients would take any medications. If the patient is told about important toxic effects and what to do about them, the physician can deal with the possibility of rare effects by simply telling the patient

to feel free to call and ask about any unusual symptoms. Many side effects are mild, may become less pronounced, or go away in time. The patients will be more compliant if they are told what to expect. If they are not told, they may conjure up visions of a serious reaction and stop the medication without consulting the physician.

#### *Patient's Attitude towards the Illness or Disability*

Illness is costly, prevents one from doing things one wants to, and is threatening. We all have resentment about being ill, and it is common for some degree of denial to be present. For many patients, taking medications reminds them of something that they would rather forget — that they are not perfectly healthy. This represents a major factor in non-compliance. It is probably the most difficult factor to deal with. A discussion about this with the patient may help.

#### *Patient's Concept of Physiology and Disease Processes*

The patient's concept of physiological functions and disease process may derive from folklore, common nonsense, or religious tradition. These concepts are usually firmly rooted and unassailable by any logic or reason an outsider can muster. A frontal assault on such beliefs is not only futile but damages relationships, and hence, compromises compliance. Further, pressing scientific views too hard upon the patient may cause the same unhappy result. Sometimes knowledge of a patient's concepts and beliefs, however erroneous we may think they are, may be turned into an asset for compliance. The patient who has firm beliefs in the importance of healthy kidneys might feel more constrained to comply with medication if it were implied that among other things, the medication would be beneficial to the kidneys. Knowing that concepts of disease are still influenced by ancient beliefs in hepatology may be of help in dealing with some patients from the Mediterranean. In dealing with compliance problems in S.E. Asians, we primarily need better communication with the patient which means ready access to qualified interpreters.

Interpreters should be able to find out what kind of health care the patient has been accustomed to and make some assessment of medical concepts the patient may hold. Some S.E. Asians have been accustomed to modern medical practice. Others are accustomed to herbal medicine and may have some religious or cultural beliefs related to the practice of medicine. It is important for the physician to find this out. For the



patient who has always relied on herbal medicine, it may help to assure him that what is being prescribed is a "purified ingredient similar to that found in herbs" and that it will perform as well or better than the herbal medicine he/she has been used to. It is important not to offend the patient by discrediting the herbal medicine practices and even acknowledge that the right herbs

may be of value; however, since the physician is well trained only in the use of his own medicine, he can vouch for its efficacy alone. Implicit here is that in allowing credibility to the patient's beliefs, he/she may then feel constrained to reciprocate and give the physician's remedy a try.

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Second Annual Competition for Bush Clinical Fellowship  
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The first *CLINICAL TOXICOLOGY* quarterly update conference will be held in the Amphitheater at St. Paul-Ramsey Medical Center on January 9, 1980. Guest speaker will be Dr. Barry Rumack, Director of the Rocky Mountain Poison Center, Denver General Hospital, Denver, Colorado. The subject of his talk will be "Acetaminophen Poisoning".

These conferences qualify for Category I CME credits and are sponsored by the Emergency Medicine Department at St. Paul-Ramsey Medical Center and the University of Minnesota Medical School under the direction of Dr. Kusum Saxena. Contact: Carol Wolf at (612) 221-3311.



# Injuries in the Runner and Jogger

Lowell Lutter, M.D.\*

Large numbers of injuries occur in the runner and jogger. Distal injuries are more frequent than injuries proximal in the lower extremities. Fifty percent of the problems were seen to be in the foot and an additional 29 percent in the knee.

Treatment plans must encompass evaluation of the abnormalities from a biomechanical standpoint with the ultimate goal of returning the runner to full activity. Specific treatments for injuries in each area are outlined.

ANY ACTIVITY in which 60 to 70 percent of the participants are injured in a given year should surely produce a major concern among the medical community. Not so with running injuries. There are approximately 10 million people in the USA running regularly,<sup>5</sup> and 60 to 70 percent of these individuals are injured severely enough each year to temporarily stop them from running.<sup>3</sup> The figures are significant, not in the seriousness of the injury, (does not require hospitalizations, surgery or medication) but in the fact that there are large groups of individuals seeking treatment to allow them to continue running.

Organized medicine has developed a bad reputation with runners. Runners' folklore says that "dogs, drivers, and doctors" are the worst enemies.<sup>6</sup> Dogs because of their injury potential, drivers because of their unpredictable habits, and doctors because of their predictability. This predictability is recommendation usually to stop running and to take some "ineffective type of treatment."

In dealing with running injuries, many physicians have forgotten that one must treat the cause of the problem and not just the symptoms. Much treatment is ineffective in that it is not directed toward the biomechanical cause. There is no lasting effect once the individual returns to high levels of running.

The underlying biomechanical abnormality must be sought and dealt with or the symptoms return. In order to deal with the primary abnormality one need not be a super specialist in the field. In fact, it has been stated that the best person to treat athletic problems is a family practitioner because of his ability to obtain a good overall picture. Surely one need not have formal education in biomechanics. One need merely fall back on the basic tenets of disease evaluation and treatment. Utilization of basic anatomy will help immensely. Identification of the injured structure(s) makes a major step in one's understanding. Treatment can then be developed on a rational basis, dealing with acute

problems and, future prevention problems.

## Materials

Increasing numbers of running injuries are seen, most likely related to large numbers of people running. Brubaker and James<sup>1</sup> review of a 17 year period of running injuries from an active sports medicine group in 1972 reported 109 injuries to runners. Our period survey of only three years, ending September 1977, was productive of 171 injuries in 121 runners. Our population was an active general orthopedic group without university age skew.

## Results

Foot and knee injuries account for 68 percent of the problems in our series. This compared to 78 percent of foot and knee problems in the survey of over 1,000 runners (Runners World<sup>4</sup>) and 48 percent in a series of University of Wisconsin study.<sup>2</sup>

The further breakdown of our series shows foot related problems accounting for half of the injuries (Table 1). Knee problems were approximately one-third, pelvis 12 percent and back 9 percent.

In the foot-ankle category, ligament or muscle

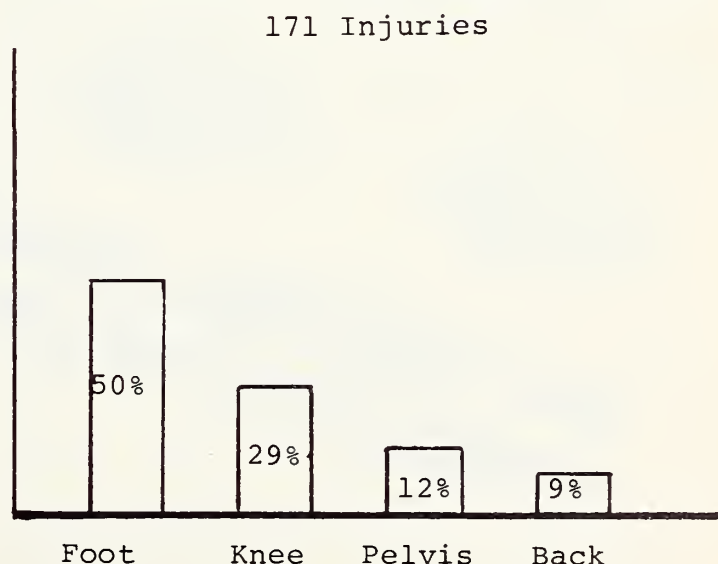


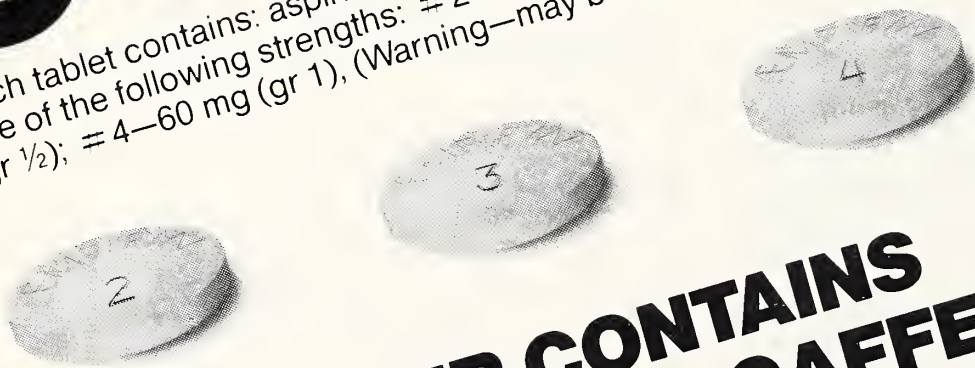
Table 1

\*St. Paul, Minnesota.



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injuries composed the largest percent, being 48 percent (Table 2) with stress fractures making up only 11 percent of the problems.

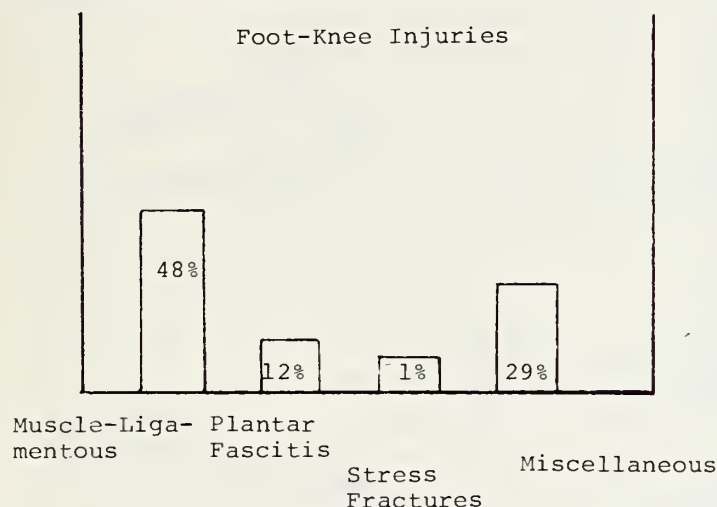


Table 2

In the knee problems, chondromalacia of the patellae was the single largest diagnosis, being 38 percent with medial and lateral ligament injuries next in amount of 44 percent (Table 3).

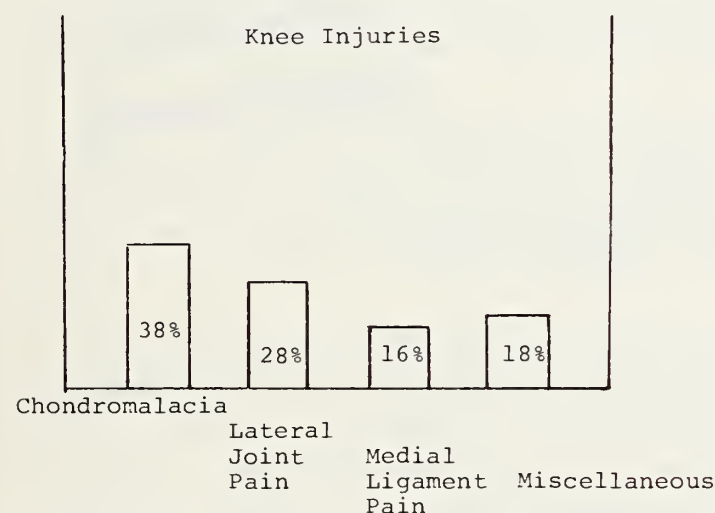


Table 3

In the pelvis-back area, there was not one specific category large enough to be splintered off.

It behooves the physician treating a large group of adult population to familiarize himself with basic foot and knee problems and their secondary effects on the pelvis and back.

## Specific Anatomic Areas

### Foot

Probably the single most important factor in production of injuries, not just in the foot, but throughout the extremities is excessive pronation. Runners who are productive of over 5000 foot strikes per hour can magnify even a small biomechanical

insufficiency into a disorder that takes him out of running.

The biomechanics of excessive pronation can be understood very simply when one looks at the normal foot at heel strike. There is some external rotation present. The pronation serves as a shock absorber and allows normal internal rotation of the limb prior to foot strike and toe off.

In the foot that excessively pronates, stress is passed upward through the foot to the knee and hip causing increased rotational motion here. In the act of walking, this is not significant, but with running there is increased weight and increased rotation which produces significant stress throughout the entire limb.

The fact that we had a gradually decreasing injury rate from the foot up to the hip implies that each joint away from the foot serves to absorb some stress. Pronation as an etiologic factor in foot problems was seen to be the cause in approximately 56 percent. The major portion of these were strains or sprains of the soft tissues and the number of stress fractures or bony problems was noted to be only 11 percent.

High arch or cavus configuration accounted for 18 percent of the total foot problems. The most consistent problem was plantar fasciitis. Pain along the long arch, particularly at the insertion of the plantar fascia into the calcaneus is what was seen. The biomechanics of this can be characterized by the "windlass" effect in which the tight plantar fascia produces stress at its insertion. This causes a stress concentration as the foot moves to foot flat. The high arch is maintained by this taut plantar fascia and the stress is then concentrated at the bony insertion. This then produces pain.

### Treatment

Treatment of the pain symptoms is generally not useful in runners. They go back to running and reproduce the same biomechanical insult, consequently, the pain returns.

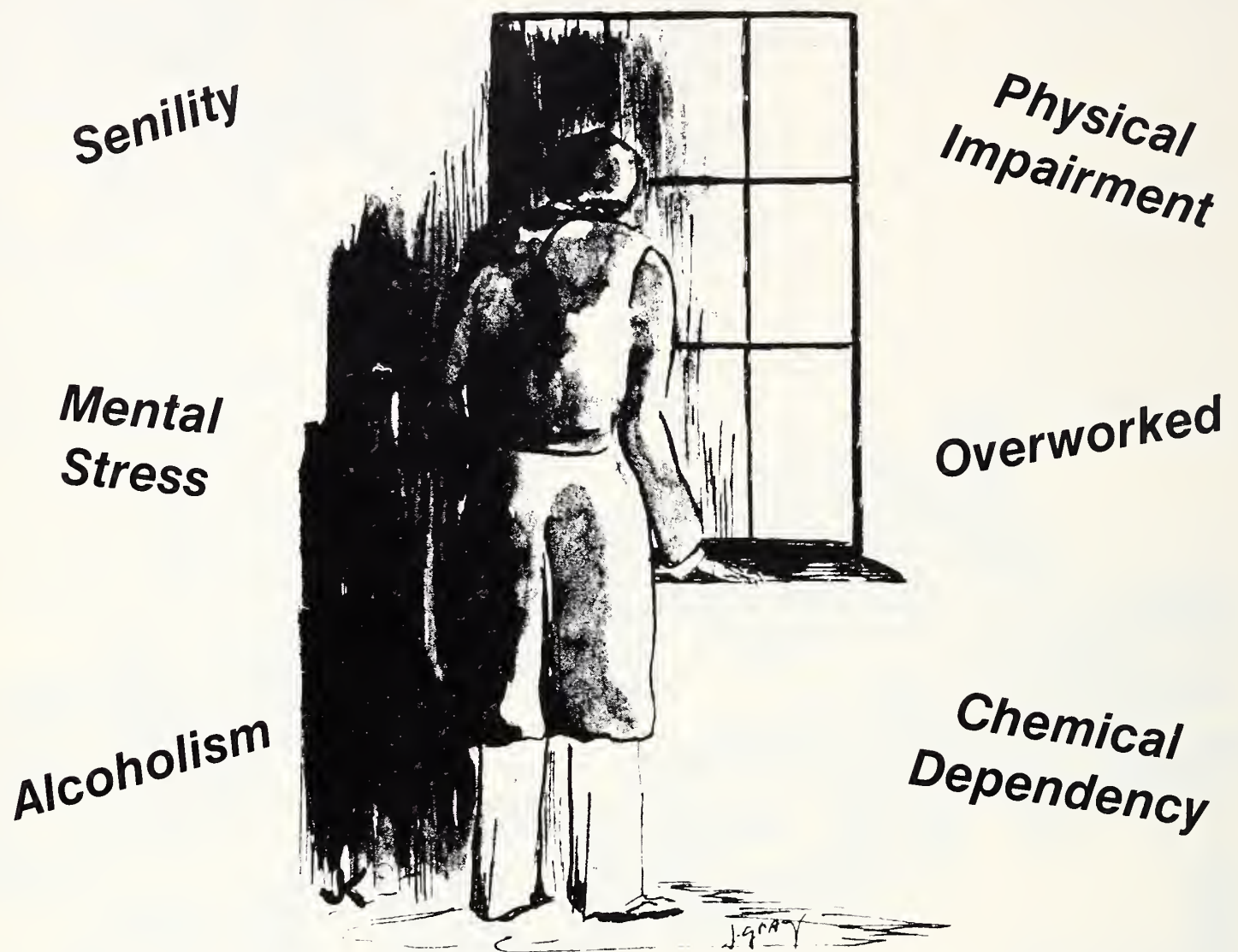
Basic treatment such as rest with long periods of time off running activities are unacceptable to runners as the first line of treatment. A very large number of runners who have seen MDs have been told by the physician that if running causes pain, one must stop.

Short term goal-oriented rest periods, while the acute inflammation is subsiding should be used. Alternative activities such as swimming and biking to preserve cardiopulmonary fitness should be prescribed. Goals should be set as to the length of decreased running, and if these are not met, then alternative treatment must be done.

Anti-inflammatory medications such as Phenylbutazolidin, have been used, but the results can be seen



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to be no better than salicylates. Currently a prescription of sustained release aspirin is felt to be as effective as any other anti-inflammatory agent. It must be spelt out in detail to the patient that this is for the inflammatory effect or your treatment again will be looked upon as "giving aspirin and showing me the door".

Contrast treatment of ice and heat works to decrease some of the inflammatory component. It should be done by the athlete through applying ice directly to the injured area after workouts and at a later time using hot soaks. Injectable steroids as the first line of treatment should be condemned. In only two cases, both of recalcitrant fascitis, were steroids used. It is felt that steroids have minimal indication in running injuries and only after exhaustion of other modalities for the expressed purpose of decreasing inflammatory reaction should they be used while biomechanical treatment is being utilized. Systemic steroids were not used.

Attention to the mechanics of the foot must be made and generally most runners require an orthosis. The orthosis most useful is one which maintains the foot in neutral position. This prevents excessive pronation if that is the underlying cause and holds the heel in neutral.

The orthosis for the cavus type of foot is designed to prevent the cavum from collapsing and stretching the plantar fascia. It is molded high into the longitudinal arch and conforms to the outline of the arch.

## Knee

Knee pain is most often related to discomfort around the patella. This can be classified as chondromalacia patellae. This plus medial ligament strain and medial joint strain constituted 54 percent of the knee complaints. These are the complaints which can be attributed generally to excessive pronation. The explanation of the excessive pronation can be seen to be a stress dissipation with the increased pronation and is noted to increase internal rotation of the tibia. When this occurs, there is excessive lateral mobility or motion of the patella. This mobility of the patella is what causes symptoms of chondromalacia. These chondromalacia symptoms generally are on the medial facet of the patella and through palpation of this area the diagnosis can be made. In addition to chondromalacia component of this, strain along the medial ligament or medial joint space can also occur from the same mechanism.

The remaining 46 percent of knee injuries were those seen from strains and sprains of ligaments and tendons.

## Treatment

Treatment of pronated related knee problems is control the pronation with appropriate orthoses. Utilization of means to control inflammation as mentioned above in the foot area is also warranted while the individual is becoming acclimated to the orthosis and is moving back into running.

Only two of the 50 knee injuries were diagnosed as medial meniscus tears. None of these were treated surgically and both returned to running activities after appropriate rest, and subsequent quadriceps strengthening and hamstring stretches. Unless a runner has a specific fall or twist, the chance of a meniscus lesion is very small. One must rule out all other causes of joint pain before performing arthrogram, arthroscopy, or arthrotomy of the knee in a runner.

## Pelvis

Injuries included in this area cover thigh and hip. The injuries tended to be strains of muscle groups attached to the pelvis. There were 18 and constituted 40 percent of the injuries in this area. They were diffuse in nature and there was no consistent theme. Only 10 percent of the injuries could be attributed to pronation and they constituted slightly more than one-tenth of the total injuries (Table 1).

## Treatment

Treatment for this group with rest, heat and anti-inflammatory medication was effective. The most important thing in terms of prevention of further problems as well as treatment of the current ones is a well performed non-running exercise program. This was a program designed to stretch the tight posterior musculature. It is well known that long distance runners tend to get tight gastroc-soleus and hamstring muscles after high level training at long distances. There is a relative over strengthening of this group of muscles with relative weakness of the anterior group of foot dorsiflexors and quadriceps muscles, consequently, an active exercise program of strengthening must be added to these.

## Back

These problems constituted only 9 percent of the difficulties in our series (Table 1). No consistent foot configuration, running style or leg problems could be identified in these individuals with back problems. They tended to be muscle-ligamentous type instead of discogenic. This was pain present with running and relieved by cessation of activity.



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## Treatment

This group of problems seems to require absolute stopping of activity for a period of time. This is much more than other areas of difficulty. No surgery was performed in this area. Extensive treatment with physical therapy and stretching was performed.

Treatment plan generally included rest with physical therapy for a short period of time. Utilization of Kraus Weber (Kraus Weber Clinical Treatment of Back Problems)<sup>4</sup> type of evaluation and exercises were instituted. Running was begun at slow, short intervals, avoiding hills, teaching the individual to run with pelvic tilt.

## Discussion

The general medical community has not been aware of runners' problems until large numbers of people began running and becoming injured.

Injury rate for running about 35 miles per week is not significant, consequently the 2 to 3 mile per day jogger will probably not require medical assistance or if so, it will be minimal and he can return to this level of functioning with minimal treatment. When an individual runs above 35 miles a week, the level of injury chance increases as high as 60 percent in individuals training for long distances over a year's time. These individuals require specific treatment for their biomechanical abnormality since they are desirous of returning to high levels of training.

The fact that many runners have delayed formal medical care, preferring to use either self-care, other runners, or paramedical personnel is based on the general lack of empathy and ineffective treatment they have felt from the medical community.

The basic tenets of any disease process hold true with running injuries. Specific evaluation of the

problem must be aimed toward elucidating the biomechanical abnormalities. The evaluation must take into effect the fact that there is most likely a biomechanical abnormality and this should be treated. The symptoms should not merely be treated. There is not a specific treatment program for each disease entity.

Treatment must be based on a rational plan which encompasses (1) activity alteration (not complete cessation), (2) pain and inflammation management, (3) stretching and strengthening, and (4) long term biomechanical control. As has been previously noted, symptomatic treatment such as anti-inflammatory medication or pain medication is rarely warranted. Surgical treatment has not been used in any of our runners and only minimal utilization of injection of steroids medication has been used.

## Summary

Injuries of the foot, knee, pelvis and back are present in large percentage of runners who consistently run 4 to 5 miles a day. These are injuries of stress or over use causation.

They are most prevalent in individuals who have underlying foot irregularities. The pronating feet, particularly with the short first toe and the rigid high arch foot, are both configurations associated with high levels of injuries. When these are identified, appropriate treatment should be prescribed which encompasses defined periods of rest, anti-inflammatory treatment, and orthosis control. The runner has found that this activity constitutes an important segment of his life and will continue to search for some appropriate treatment which allows him to go back to this level of functioning.

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# Rheumatology Corner

## Gold Therapy in Rheumatoid Arthritis

GERALD T. MULLIN, JR., M.D.\*

Gold is a potent inhibitor of the inflammatory response in rheumatoid arthritis (R.A.). If given to the proper patient, it can slowly suppress the disease, stop synovial proliferation, and avoid destruction of joints and tendons. Two-thirds of patients with R.A. will show improvement greater than expected without the use of gold.

### Patients to treat:

1. Those with early R.A. (present continuously 6-9 mos. without remission).
2. Those unresponsive to rest, physical therapy (P.T.), aspirin, or nonsteroidal anti-inflammatory drugs (N.S.A.I.D.).
3. Those with a lot of palpable synovitis on exam, with beginning destructive changes on x-ray.
4. Selected patients with severe psoriatic arthritis, juvenile R.A., or palindromic rheumatism.
5. Those with advanced R.A., who show continuing synovial proliferation.

### Patients not to treat:

1. Those with little active synovitis.
2. Previous gold failures (known adequate dose).
3. Those with previous severe gold reactions.
4. Those too impatient to wait for drug to work.
5. Those with unrelated, severe renal disease.
6. Those with osteoarthritis, S.L.E., or ankylosing spondylitis.

4. More effective and less toxic than imuran, cytoxan, or chlorambucil.

### Patients must understand that:

1. Efficacy is noted very slowly and infrequently before 6 to 8 weeks.
2. ASA or NSAID must be continued when using gold.
3. Laboratory monitoring is imperative.
4. Reporting of possible side effects is very important before next injection is given.

### Drugs available:

1. Intramuscularly injected drugs, usually in buttocks.
  - (a) Myochrisine (gold sodium thiomolate) — water soluble and easy to draw up; occasionally causes nitritoid reactions (flushing, rhinorrhea, or fainting immediately after injections).
  - (b) Solgonal (aurothioglucose) — oil soluble; more difficult to draw up in syringe; may be less toxic than myochrisine.
2. Oral gold — auranofan (triethylphosphine gold) — promising drug, but experimental now in USA.
3. Intra-articular gold — no more effective than intramuscular injections.

Remember: Serum levels don't correlate with clinical improvement, and neither does the size of the individual dose or cumulative amount.

A treatment schedule: 15 mg 1st week; 35 mg 2nd week; 50 mg weekly thereafter to 1000 mg; then go to prolonged maintenance therapy (see below).

Remember: The first dose can infrequently give a severe reaction.

### 1. Careful questioning before injection:

- (a) Mouth sores, metallic taste, stomatitis — most frequent early warning of side effects in my experience.
- (b) Any rash not usual to patient (usually very itchy); "Minnesota winter itch" difficult to

Personal biases comparing gold with other long-term suppressant drugs:

1. Less toxic than penicillamine; therefore, to be tried first.
2. More effective than antimalarials.
3. Less effective in patients on steroids.

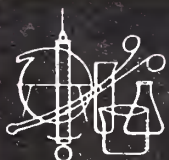
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sort out — photosensitivity reaction may occur.

2. Laboratory parameters checked before injection:

- (a) Weekly urine for protein. 1+ proteinuria and more — stop until it goes away and resume gold at lower dose.
- (b) White blood cells with platelet estimate from smear. Do weekly to 12 weeks then every other week to 20 weeks, then every third injection.
  - (1) Thrombocytopenia most common hematologic side effect — no correlation with mucocutaneous or renal side effects.
  - (2) Leukocytosis above 15,000 — sudden rise, if not explained by infection or concomitant steroid administration. Watch for reaction.
  - (3) Leukopenia under 3000 — hold dose until it rises. Assess in light of previous leukopenias present with RA.
  - (4) Eosinophilia — sudden rise may mean impending reaction, but some patients with RA run persistent eosinophilia.
- (c) Hemoglobin — need not be checked each time. A good lab parameter to follow improvement — as good as sed rate.
- (d) Liver function test (SGOT) — done twice yearly. Infrequent hepatic reaction seen.

Remember: If in doubt about a potential reaction, be safe and omit the dose.

Maintenance gold therapy after original loading dose:

- 1. Gradually spread out time interval from 2 to 4 to 6 weeks. Give indefinitely at 50 mg per injection.
- 2. With disease exacerbation go back to weekly or twice monthly doses until the disease is better controlled; then spread out again slowly.
- 3. If mouth or skin reactions occur at low dose, such

as 15 to 25 mg., give half this dose at 2 to 4 week intervals until effect on disease is seen or not seen.

- 4. If in complete remission for a year, the drug may be stopped. (Many rheumatologists prefer to give drug at prolonged intervals even then.)

Remember: Loss of benefit may occur after 4 to 6 years. In one study from Columbus Medical Center, only 15% of patients were still on the drug after 4 to 6 years. My experience is similar.

Gold and other drugs

- 1. Continue corticosteroids at previous dose. Reduce slowly when the gold effect is seen.
- 2. Gold may be combined with antimalarial drugs such as hydroxychloroquine, but additive efficacy has not been proved.

Treatment of toxicity

- 1. If severe mucous membrane lesions occur, stop drug, and, when clear, restart at lower level.
- 2. Exfoliative dermatitis: Use systemic corticosteroids to control symptoms. Don't resume gold.
- 3. Proteinuria: Stop drug until clearing; then resume at lower dose.
- 4. Thrombocytopenia: Use systemic corticosteroids (occasionally must be continued for a long time). Don't resume gold.

Remember: Chelating agents such as penicillamine or BAL are not effective in treating toxicity and are potentially toxic themselves.

Gold can be found in the laboratory to reduce many parameters of acute and chronic inflammation. Inactivation of sulfhydryl-dependent enzymes is probably the most important one. For the clinician, however, it is most important to know how to use the drug correctly, which patients to treat, and how to identify and avoid reactions.

### Continuing Medical Education

#### Seminars in Rheumatology III

Hilton Hawaiian Village, Honolulu, Hawaii — February 20-27, 1980

**ACCREDITATION:** As an organization accredited for continuing medical education, the Minnesota Medical Association designates this continuing medical activity as meeting the criteria for twenty (20) credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association. Program also acceptable for prescribed hours by the American Academy of Family Physicians.

Contact: North Central Medical Conference, Suite 900, American National Bank Building, 101 E. 5th Street, St. Paul, MN 55101 • Tel. (612) 222-6366.



# Minnesota Medical Association

## CME Evaluation

### 1979 Minnesota Medical Annual Meeting

DONALD R. HOUGE, PH.D.\*

THE PAST MMA Annual Meeting offered the largest selection of Continuing Medical Education courses ever offered at an annual meeting. Dr. Stuart Thorson, Chairman of the Medical Education Subcommittee on Scientific Assembly, issued the challenge: "How do we know the programs meet the physicians' needs? Are we offering quality programs? Can we do a sound evaluation without overburdening the participants? How can we obtain information to help faculty to improve their teaching? Can we have a report that is useful in guiding our efforts and lastly, can we develop a process that allows us to incorporate the evaluation results into our planning and decision making?"

In response to these questions, Dr. Douglas Fenderson, Lois Fossum, Dr. Stu Thorson and the author developed an evaluation package with several components: (1) Participant evaluation of the overall program, (2) Participant evaluation of the specific courses, (3) Participant/observer evaluation of the courses, (4) an evaluation report to planners, (5) evaluation information for faculty, (6) an evaluation review process, and (7) a report to the membership.

#### The Overall Program

In terms of general satisfaction — the participants were pleased. Ninety-three percent of the physicians indicated that it provided sufficient variety to meet their needs and interest, and 98 percent evaluated the meeting as either good or excellent.

Specific program strengths were identified as quality of faculty combined with a good selection of topics. Areas for improvement suggested by the participants centered around improvements in transportation, and seating, lighting and acoustics for some of the individual courses.

The format of the scientific program — with its emphasis on three hour educational programs as contrasted to large plenary sessions — was given strong support by the participants with less than two percent indicating a need for change.

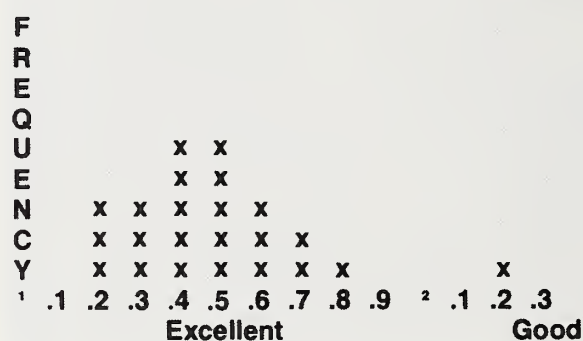
#### Individual Courses

Individual courses were rated by the participants on

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several dimensions. One question asked the participants to evaluate the course in general terms on a scale from Excellent to Poor. The figure below shows the ratings for 23 of the individual courses. As shown in the figure, only one of the courses had a mean rating less than 1.8. These results indicate a high level of acceptance when compared to other CME courses offered throughout the state and country.

**Average Ratings for Courses**  
(each x represents a course rating)  
Scale goes from 1 to 4 with 1 being high.



No ratings were below 2.2 and ratings go from 1 = Excellent to 4 = Poor.

The courses were rated on four dimensions of course content and methodology. Although there was variability within course ratings for the courses, the participants placed the most value on the "basic concepts" that were presented.

Participant/Observers (P/O) were also assigned to each course. The P/O is a new evaluation technique that was tried this year on an experimental basis. Using this technique, physicians were selected in advance from the course participant list and given specially designed questionnaires to evaluate aspects of the course that go beyond that which is usually asked of participants. Questions that dealt with aspects such as the flow of the course, physical arrangements, participant interaction and reaction during the course, and the degree to which the course met its stated objectives were particularly useful. The reports filed by the P/Os were then used as supplemental data to the summarized participants evaluation. Each P/O was asked for his or her opinion of the usefulness of the technique. Their comments indicated that they felt the



technique was a valuable addition. Some typical comments were "Good idea to hopefully monitor the quality of the course and improve upon the quality", "The key is to be frankly critical", "Should result in a continual upgrading of presentations".

Each individual speaker at each course had his or her teaching evaluated on three dimensions by all course participants. The dimensions were: (1) quality of presentation. Participants were told to consider speaking expertise, organization and use of visual aids in rating speaker on this topic. (2) level of content presented. Participants were told to consider the practicality of the information on a continuum from "too esoteric" to "too basic" and (3) value of topic. Participants were told to consider the value of the topic to them independent of "level of content" and "quality of presentation". These three dimensions have been used in several continuing medical education courses and have been found to be relatively independent of each other. Course faculty have indicated that receiving information on these three dimensions have allowed them to have a better understanding of how their presentation was received rather than through the use of the more commonly used "global rating". It lets course planners know: (1) the value of specific topics within a content area as well as (2) whether their overall goals in terms of content are too esoteric or too basic and (3) the degree to which programs need to be developed to improve the teaching skills of the presenters. In addition, each course was evaluated on four aspects related to content and five aspects of methodology.

The courses rated the highest had clearly stated objectives and faculty that addressed the objectives in a fashion that focused on practical clinically useful information. In addition, those courses that had well developed abstracts and teaching aids also received

high ratings. The three most highly rated courses were: Dizziness — A Panel Discussion by Drs. Melvin Siegel, A. B. Baker, H. M. Paisner, Robert A. Van Tassel, Practical Skills in Surgical Management by Drs. Lynn Solem, Jeffrey Howe and Herbert Crandall and Update in Clinical Virology by Drs. Henry Balfour and Gilbert Schiff.

### **Evaluation Report**

A final 64 page evaluation report covering the overall program evaluation, the participants evaluations of courses, the participant/observer reports, the procedures used for selecting courses and participant comments was sent to each member of the education subcommittee, and Dr. Robert Avant, new chairman of the medical education subcommittee on Scientific Assembly. Each course director was sent a summary of his/her course evaluation results.

### **Importance of Evaluation**

Evaluation of CME courses is becoming increasingly important as a means of providing quality programs for the busy practicing physician. The practicing physicians evaluation forms are seriously reviewed. Course planners are increasingly using the evaluation data to make decisions about future courses. Individual course faculty also are asking for this data. Our experience shows the course faculty are striving to improve upon their teaching and want data that helps them to do so. Honest, frank appraisals of courses by the practicing physicians can help in this process. It is strongly urged that the practicing physician take the time and responsibility to carefully review each course he/her participates in and to turn the forms in at the completion of each course. The results are improved educational programs and accountability to the membership.

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1980 Minnesota Medical Association 127th Annual Meeting  
May 20-22  
Radisson South — Bloomington



# Conversation with Dr. Merle Mark, Chairman of the MMA Committee on Legislation



Dr. Richard L. Reece (left)  
and  
Dr. Merle Mark (right)

**Dr. Richard Reece:** Dr. Mark, what is your official position in the Minnesota Medical Association?

**Dr. Merle Mark:** Chairman of the Committee on Legislation.

**Dr. Reece:** How long have you held the job, and what is your background in legislative activities?

**Dr. Mark:** This is my second year as Chairman of the Legislative Committee. I inherited the chairmanship from Chet Anderson from Hector. Before this, I was Legislative Chairman of the State Academy of Family Physicians and was active with MINNPAC. Then, on my own, I had participated in state politics.

**Dr. Reece:** Do you regard your function as vital to the Association?

**Dr. Mark:** Legislation is of prime importance to the State Medical Association and to private medicine.

**Dr. Reece:** How do you determine the Association's legislative policy?

**Dr. Mark:** It is a grass-roots affair, and it varies. Any physician can call me on the phone or write and say "There ought to be a law." Or, from the other extreme, bills are introduced, and we determine if they are of sufficient priority to devote time to. We receive letters and bills from our state representatives and senators and some from the Health Department. We try to respond and make recommendations on all important health related proposals. However, the MMA House of Delegates and Board of Trustees ultimately determine Association policy. It is then up to the Committee on Legislation to implement their decisions.

**Dr. Reece:** Do you lobby yourself?

**Dr. Mark:** As little as possible. This differs from my predecessor, Chet Anderson, who is really my inspiration. He would spend a day a week away from his solo practice in Hector to lobby. I have tried a different thrust. I feel the more people involved, the better. So I spend as little time at the State Capitol as possible. With the help of staff, I try to get other physicians involved. In this last session of the legislature, I appeared once or twice to testify as a spokesman for the Association. Jim Sova, our lobbyist, recruits medical experts in those bills we deal with, to testify. How much time I spend a week on legislative matters? I would say one to two days during the sessions, one-half to one day during the interim. Our Committee meets year around.

**Dr. Reece:** You have been a busy family practitioner in a five-man group in Crystal for twenty years. That experience must give you a special perspective on the health care system.

**Dr. Mark:** I think so. I was born and raised in North Minneapolis, now considered a ghetto. At that time, we were all poor, and so poverty meant little to us. So I can relate to the have-nots. Also, I have a minority background, and feel I can appreciate the areas of need for good health care. As a family practitioner, I am out in the trenches.

**Dr. Reece:** Could you define more precisely the Association's lobbying activities and how these are carried out?

**Dr. Mark:** We are blessed with the best lobbyist on the hill, Jim Sova. He is ably assisted by Chuck Wiger. As



issues come up, they buttonhole various legislators to share with them the views of Minnesota Medical Association. They constantly consult with 201 legislators over there as well as with lobbyists of other special interest groups. Also, they are in contact with the staffs of the various committees which hear legislation dealing with health care. Last, but not least, lines of communication are maintained with the Governor's office and also with the Commissioner of Health and the Commissioner of Public Welfare. Through these concerted efforts, they attempt to present medicine's view. They are ably assisted by a network of contact physicians throughout the state, physicians such as myself, who for want of a better word, bird-dog legislators when they are at home in their districts.

I attend political pancake breakfasts, speak to politicians during their public library hours and sometimes go over to the State Capitol to talk to them. This is a concerted lobbying effort.

**Dr. Reece:** Most people would agree times are changing. A conservative drift is occurring. Take Proposition 13. Has this more conservative atmosphere affected your lobbying activities?

**Dr. Mark:** I have seen subtle changes as far as funding bills is concerned. We are seeing fewer way-out bills. But I'm not sure ideology makes much difference. I would like to think that every single legislator over there is an honest, hard-working, sincere person trying to do the best job he or she can. Our job is to catch their ears and share medicine's view so that they can make an intelligent decision on health related issues.

So any great differences as a result of the Proposition 13 referendum have been subtle. We don't see too many bills that look for pie-in-the sky funding, but there have never been many bills like that. Minnesota, despite the many liberal politicians who have been spawned here, is a conservative state. The Democrats here that we would think are pretty liberal, would be considered conservative in the Democratic party bastions elsewhere in our nation.

**Dr. Reece:** A bill is now in Congress to curtail the political action committees, the PACs, because critics feel these committees represent too much power for vested interests. Do you think that MINNPAC has too much power? Or not enough?

**Dr. Mark:** I'd rather use the word "effectiveness" instead of "power." MINNPAC has been effective through the years, but not nearly as effective as it could be if more physicians supported it. Any legislation to curb or restrict PAC activities, I believe would be a gross infringement on the rights of individuals to collectively organize for political purposes. MINNPAC represents a potent lobbying aid for the Medical Association, but let's make it clear that these are separate organizations. It is no different when you are talking MINNPAC and political action than if you are talking COPE, the political action committee of the AFL-CIO, or IMPACE, the teachers' PAC organization. MINNPAC is unique amongst many of them, I would say, in that it is truly bi-partisan. I don't have the figures on the tip of my tongue, but in the last state races, MINNPAC was on record as supporting almost as many Democrats in races as Republicans. MINNPAC serves a dual function: (1) It tries to help elect legislators who are willing to listen. This is all we ask or MINNPAC asks, that MMA representatives are given the ear of the legislator. (2) MINNPAC encourages physicians and their spouses to organize candidate support activities.

We would like to see 201 legislators who will listen before they vote and who are willing to spend the time broadening their perspective on health matters.

When politicians are elected to office, they remember that MINNPAC contributed to their campaign just as they remember that other groups contributed to their campaign. If you call and say you would like to talk about a bill, they usually will be willing to listen whether they agree with us or not.

**Dr. Reece:** As you know, the Association reorganized three years ago with more emphasis on legislative affairs. Any impact?

**Dr. Mark:** It is not only emphasizing legislative affairs, but the whole gamut of socio-economic affairs of which legislation is only one part. The Association's reorganization was a good thing. It was a vital and necessary thing. I would like to think that it has been very successful.

**Dr. Reece:** What do you think are the key issues faced by organized medicine in the 1980s in the Minnesota legislature?

**Dr. Mark:** Several of these are issues that we have dealt with before. Even though we may have successfully dealt with them, bills never really die; they smolder like fires in peat bogs and come back to haunt us in the next



session. The effort of chiropractors to broaden the scope of their practice is a good example. The chiropractors, as you probably know, have a three-pronged effort.

Number one, the faculty of the chiropractic school has chutzpah, a good Jewish word, which means incredible guts. They said to the legislative interim committee touring the chiropractic campus that students, when they graduate, are as well trained as any family doctor in this state. Chiropractors feel that they are as well trained as you or I and therefore they should be free to practice as you and I under the law.

Number Two, chiropractors feel that they are entitled to hospital privileges.

Thirdly, chiropractors feel that their schools are as entitled to educational funds as any medical school. They don't spare any lobbying effort to get that across.

There are constant attempts by well-meaning people who feel that private medical records should be public or that if not public, should not at least be private and confidential, but should be someplace in between. This is a repetitive thing.

Health planners have tried to extend certificate of need regulations to physicians' offices, to prevent us from purchasing diagnostic and therapeutic equipment costing over \$150,000. So far they have been unsuccessful.

**Dr. Reece:** What is the status of the Certificates of Need for physicians' offices?

**Dr. Mark:** As far as physician offices are concerned, unless physicians are in collusion with the hospital, it is not necessary to apply for a Certificate of Need. Recently enacted federal legislation, however, will require a Certificate of Need if equipment costing over \$150,000 is used for hospital inpatients in physicians' offices or clinics.

I can foresee where Certificate of Need might be extended to physician placement. If you wanted to ask a pathologist to join your group, you might have to apply for a Certificate of Need, because there is a doctor or hospital outstate that doesn't have the services of a pathologist and therefore the next pathologist who wishes to be licensed in this state will have to go out there. It may sound ridiculous, but it is conceivable.

**Dr. Reece:** So there may be efforts to dictate where one practices.

**Dr. Mark:** These may sound like pipe-dreams, but bills of this effect are pending in some states now. Other issues that we are going to have to deal with are efforts to regulate psychosurgery; a bill which would require physicians and facilities where such surgery is performed to conform to a complex procedural reporting requirement under the aegis of the Health Department. MMA was able to diffuse this issue during this interim, however, by establishing guidelines for psychosurgery and asking hospitals' medical staffs to adopt them if they performed this procedure. In view of our efforts to strengthen internal peer control of psychosurgery, the bill's author did not bring the issue up for vote.

The fact remains that if this bill were enacted, it would establish a dangerous precedent. If you had to go through a complex procedural and reporting requirement for psychosurgery, then the next step would be to add gastric by-passes and gastric staplings, and then on to mammary reductions et al. It would be detrimental to the private practice of medicine to have state laws and statutes regulate what we can do and what we can't do.

The issue of health screening is going to be looked at by the state legislature for state employees as well as pre-school screening for children.

There will be efforts to modify and drastically change HMO requirements. There will be efforts by other allied health professionals to be mandated as HMO providers, not only optometrists but also chiropractors. One of the secrets of success of the HMO concept is its ability to be cost effective and have ongoing peer review to assure quality of care.

If allied health professionals were mandated as part of the system, it would just tear HMOs apart.

**Dr. Reece:** Any other big issues?

**Dr. Mark:** The Association, as you know, is on record at the House of Delegates as in favor of legislation which would codify the concept of brain death so that we would be consistent with several other states who have on their books uniform brain death laws.

The House of Delegates at the last annual meeting felt that it was essential to have a bill which recognizes brain death. It is a simple bill. What it says is that a person is legally dead when his brain and brain stem cease to function. The Association received a lot of flak from pro-life people who said that this was a backdoor to euthanasia or abortion, which is obviously not true. We got flak from people who felt it was tantamount to killing grandpas and grandmas. I even got a call from an antivivisectionist who told me that I was against cats



## CONVERSATION WITH DR. MERLE MARK

and dogs because that is how they eliminate cats and dogs. Brain death is an important issue, and it is important for us to see it through to fruition in this state.

Something that bothered me last year were innuendos by the Welfare Department that doctors are scurrilous characters who need to be closely supervised. They attempted to get a bill enacted into law which would have judged us before we had our day in court. The bill assumed that most doctors are guilty of fraud and negligence in dealing with welfare patients. The bill would have permitted them to sweep into our offices at any time and demand to look at a welfare recipient's records right then and there to determine if fraud was being enacted or the treatment was medically necessary. To our dismay, the majority vote on that subcommittee agreed with them. Fortunately, a prior notification safeguard was later reinstated, however, a House floor fight on this issue can be expected this session. This demonstrates an underlying mistrust of medicine. You know the old saw, "I trust my physician with *my* life, but the rest of you doctors I'm not sure of."

These are some of the issues that we may see. We may see efforts to negate the Treatment of Minors Act which the Association worked hard for in the early '70s. By this Act, you and I, in private practice, could treat a minor in confidence. They wouldn't have to have their parent's permission or prior knowledge, so that we could treat them for venereal disease or advise them as to an unwanted pregnancy and steer them to an appropriate, sound health care resource to deal with the pregnancy.

Efforts have been made to gut the Treatment of Minors Act. Minors would once again have to get their parent's written consent to be treated or at least have their parent's prior notification. If that were to happen, we would be back, I am afraid to the old abortion mills and to rampant VD in teenagers.

**Dr. Reece:** Medicine's critics charge we are defensive on the issues. Any comment?

**Dr. Mark:** Not true. That is not true. Last session we sponsored a bill which would establish a poison information center for the State. Anybody in the state could call a number, toll-free, any time of the day, seven days a week, fifty-two weeks a year, be he or she a social worker, a law enforcement officer, a health care professional, hospital or parent, to get information on any poison or potential poison. The bill passed the Senate, but unfortunately, there is no money to fund it as yet in the House.

The Association attempted to reinstate the motorcycle helmet law, and it did not pass. The Association tried to enact a law which would help restrain children in vehicles, but it did not pass. We pioneered and underwrote a key study on water quality by the Freshwater Biological Institute at Lake Minnetonka.

The Association, in the past, has had the reputation, ill-deserved as it may be, of always being opposed to things. Over the last few years, I have seen many issues on which we were the advocates.

**Dr. Reece:** Let's take something more fundamental: the alleged mal-distribution of physicians. In your experience as a past Vice President of the Academy of Family Physicians and with the state legislature, what has organized medicine done to remedy this problem?

**Dr. Mark:** I don't accept the basic premise of a mal-distribution. I am the wrong man to ask what the Association is doing. I am, however, familiar with what the Academy of Family Physicians is doing. Scores of family doctors throughout Minnesota hold clinical teaching positions with the Department of Family Practice at the University and participate in the rural physician-rural student training programs. Medical students spend up to a year with a physician practicing outstate. Most of them are so stimulated by what they see, that they go back to the same rural area to practice when they graduate. Both the MAFP and the MMA supported these programs.

**Dr. Reece:** Do you agree Minnesota should be proud of its growing number of family practitioners?

**Dr. Mark:** Yes. Minnesota is a traditional bulwark of family practice. Several of the national officers of the American Academy of Family Physicians are currently practicing physicians in this state. Many other Minnesota family physicians serve in key roles in the American Academy of Family Physicians.

**Dr. Reece:** So you would say the primary health care in the state of Minnesota is solid.

**Dr. Mark:** Yes, sir, thanks to the dedicated efforts of many physicians who sought to establish a strong family practice department at the University, a medical school in Duluth, a family practice program there, and a medical school in Rochester at the Mayo Clinic with a family practice division there. Thanks too to the many physicians who, with no pay, take students as preceptors.



## CONVERSATION WITH DR. MERLE MARK

**Dr. Reece:** Do you regard these activities as a tribute to the cooperative enterprise of the Minnesota physicians?

**Dr. Mark:** No question about it.

**Dr. Reece:** How can we stimulate even further political participation by the medical community?

**Dr. Mark:** We can do that by the publications that the Association puts out, the Physician's Legislative Bulletins, Newpage, MINNESOTA MEDICINE, Physician's Alert, the various county society publications and a legislative committee representing physicians from all parts of the state. We can also use that marvelous resource, our spouses in the State Auxiliary. Lastly, we can stimulate participation by maintaining effective lines of communication with the other organized bodies of physicians practicing in Minnesota.

Last summer, Jim Sova and I sent letters to every county society saying: "Have spiel, will travel." There are over 30 county societies in our Association, and 15 have invited us to come and speak to them. To the ones way off, we fly. As the weather gets unpredictable, as it will by the time the legislature convenes in January, we will have flown as far as Fergus Falls, Worthington, Montevideo, and Hibbing. We will speak to county medical societies and auxiliary chapters trying to spread the gospel of the need for physician involvement in the politics of health care. I would like that message to be the keynote of this interview.

**Dr. Reece:** Do you wish readers to extend an invitation to you and your colleagues to speak to them: weather, family and practice permitting?

**Dr. Mark:** You betcha! Although we can't really go once the legislature is in session, because things happen so fast over there that we can't promise to show up.

**Dr. Reece:** When does the session start? When does it end?

**Dr. Mark:** January to May. The sessions are biennial, the first year is January through May and the second year, January through March and sometimes into April. Summer, fall and early winter. We still find apathy in this state and perhaps always will. But I hope that it is on the decline. Less than 25% of the members of the Association are members of MINNPAC, I'm sorry to say.

We were in Fergus Falls a couple of weeks ago, and one doctor raised his hand and said, "You know, I think that you fellows are all wrong. You should just stay by the wayside and let health care go down the drain and then people will come to you on hands and knees and say please resurrect this for us, won't you."

I told him that that was about as short-sighted a view as I would ever hope to hear and that the days of putting our heads in the sand have gone.

**Dr. Reece:** Would you agree that comprehensive health care, once enacted, is irreversible?

**Dr. Mark:** Yes, Sir, if you mean National Health Insurance. Experts far wiser than I have said that, including legislators at the state capitol. Now is always the time to fight the battle. I subscribe to the philosophy that today is the first day of the rest of my life, and that means my professional career as well. That means the health care that I feel that my patients deserve. It is important to distinguish between fallacy and fact. Many well-intentioned, but confused, people say that the citizens in this country are entitled to health care; that they have a right to health care. I think that is a fallacy. People in this country have the right of *access* to health care, and that is an important distinction.

**Dr. Reece:** How so?

**Dr. Mark:** Well, I think that the patient shares the responsibility for health care with his physician. The patient shares the responsibility so that you have a more informed, more well motivated, healthier patient. You also have a more well-motivated and sound physician. Patient and physician go hand in hand. It is important that physicians be involved right at the grass-roots and right on through to where the bills become enacted into law.

**Dr. Reece:** Do you believe in a pluralistic, competitive medical system with a place for private practices, group practices, HMOs and public institutions?

**Dr. Mark:** There are many pathways to good health care for patients. My own private practice is a good example. We have private patients and those that receive public funds. We are members of the Physician's Health Plan and we also have many patients whom we treat for nothing. We know that they will never be able to pay and we are happy to take care of them.



## CONVERSATION WITH DR. MERLE MARK

**Dr. Reece:** So you believe in diversity and flexibility?

**Dr. Mark:** Yes, that makes for a healthier tomorrow.

**Dr. Reece:** Dr. Mark, could you describe the make-up and activities of the Minnesota Medical Association Committee on Legislation?

**Dr. Mark:** The Committee on Legislation is composed of one representative from each of the eight Congressional Districts in the state. In addition, there are three members at large.

Issues are brought to us, as I mentioned earlier, by member physicians or allied health people, public officials and concerned citizens who write to us or otherwise communicate. We consult the staffs at the Department of Health and the Department of Public Welfare and discuss health issues. We also consult with the Governor's staff people. The last session of legislature saw over 2,000 bills introduced. Of those, some 400 dealt in some way with health care. Our able staff looked at better than 200 of these in great detail. We, as a committee, assigned priorities and looked at some 60 or 70, offering testimony and monitoring them as they were heard in various committees and as they were either defeated or enacted into law.

We had continuing meetings with the legislative assistant in the Governor's office and with our counterparts at the state hospital association. Often we do not agree on the issues, taking opposite sides on some, but we feel that it is better for us all to share our views. We then act upon the bills that are presented to us and recommend action to the Board of Trustees. The Board determines policy, and the Board appoints the members of the Legislative Committee.

**Dr. Reece:** What direction do you see in health legislation in the next decade?

**Dr. Mark:** Continued efforts by organized medicine to promulgate bills that improve the health care delivery system. Efforts by the consumer to make health legislation effective and practical and to fill voids of need as they see them and to better health care delivery in areas that they feel are not efficient. I see more conservative attitudes by the legislature on government regulations and the funding of various bills. I would like to see a more active physician and physician-spouse involvement in health legislation. I'd like to see more physicians run for state office. We need more physicians, like Dr. Sommerdorf from St. Paul and Dr. John Salchert from Minneapolis, both of whom served for several years in the state legislature. Now Dr. Robert Reif, is serving his first term for his district of White Bear Lake. In the state legislature are dentists, veterinarians, chiropractors, and social workers, as well as other professionals such as lawyers, educators and journalists. More physicians though should run for office.

**Dr. Reece:** You are a good family man, a good father, and an excellent physician, why are you so involved in politics?

**Dr. Mark:** I'm involved, because of the inspiration that has been given me by doctors long a part of politics in this state. Ed Luh from Fergus Falls got me involved in MINNPAC when it was still known as Nuhope. My biggest inspiration has been Chet Anderson from Hector, who has been my father-figure in medical politics. It is a labor of necessity; it's not a labor of love. I view myself as just one in a series of legislative chairmen, starting with John Falls, Chet Anderson, myself and long after me other MDs as we try to get more physicians to participate.

As I have said before, ideas get enacted into laws whether we are there or not. If we are there, we can directly affect what a bill does and how practical and solid the law is. We can modify a detrimental bill, and can encourage enactment into law bills that are good for health care. We can work with other health professionals to push issues we feel are important for us and for our patients.

One final word. February 1980 is political caucus time in this State. I would hope that others in medicine will see the need for involvement as I do and attend their precinct caucuses be they Democrat or Republican. Be involved. Politics *are not beneath* the dignity of our profession. Politics *is* the name of the game.



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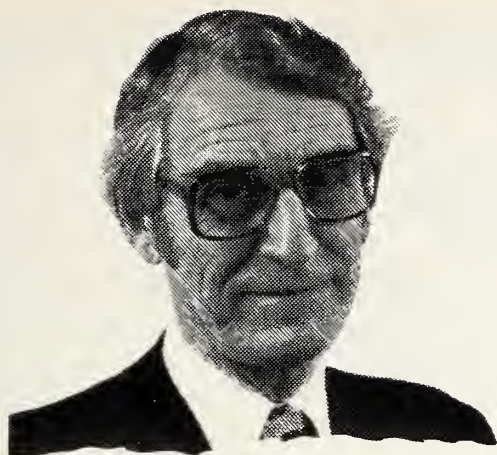
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## President's Letter

A generation ago, physicians practiced without appreciable threat of litigation. Claims were relatively infrequent, and in the vast majority, those filed came as a result of patient injury clearly due to an error of commission or omission. Professional liability premiums were modest and gladly paid by the physician, since they were viewed as providing justified compensation for avoidable injury. During this period, except for rare and unusual situations, patients and families related to a single physician. It was natural and normal for the patient to select a physician whose personality as well as cultural, ethnic, and religious background agreed most comfortably with his/her own. It is easy to see how, in this situation, the physician often came to be regarded as "one of the family" and as a result enjoyed the full trust and confidence of his patients. It is also easy to see how, in this situation, the thought of malpractice litigation did not come easily to the patient's mind. All of this however, is in the past and seems lost to us for the foreseeable future.

Today, comprehensive medical care cannot be rendered by a single physician. The knowledge, techniques, and skills necessary are more than the most expansive among us could hope to gather to himself or herself. Thus care is often fragmented as we are directed from one specialist to another in pursuit of a diagnosis or treatment. The specialist understandably concentrates on his/her area of expertise and may not give proper emphasis to the whole person. The necessary concentration of specialized talent and technology in the impersonal climate of an urban center does little to strengthen the physician-patient bond. When the specialist is also one who comes from a foreign culture, and may even have a language barrier, it is easy to see how misunderstanding arises. The feeling of a close patient-physician relationship being absent, such misunderstandings often lead to litigation. The situation as it exists is, however, a fact of life.

In order to better serve ourselves and our patients, we must adjust as quickly as possible to the changing

scene in professional liability litigation. This means that we must always keep in mind and attempt to convey to the patient that we are interested in the whole person and not just the disease process. Society demands and good practice dictates that our records clearly, concisely, and accurately relate the story of the care we have given our patients. We must be active in peer review and participate in the educational effort to improve quality of care or correct deviant practice.

Thus far I have simply asked that we improve upon and perfect all of the things that we already are doing. Beyond this, however, I think we must all make ourselves knowledgeable about the adversary system of justice, so that we may be comfortable and effective in a court setting. There must be close cooperation between the defendant physician, the insurance carrier's claim agent, and the defense attorney in order that the truth be adequately displayed. We must learn to give medical testimony in a straight forward factual manner. Super specialists should keep an awareness that the highly developed, finely honed skills, which they possess, cannot realistically be expected from those physicians engaged on the broad front in day-to-day office practice. In this regard, those from well known institutions, or academic settings, have a particularly great responsibility when they testify as expert witnesses, since their word reflects not only their personal stature but carries with it the prestige and weight of the institution which they represent.

In order to keep abreast in these changing times, let us henceforth take advantage of every opportunity to inform ourselves at the various medical-legal symposia and seminars. As your President, I have reason to hope that your MMA will find it possible to become increasingly involved in this important area of our practice to the benefit, not only of its members, but of the patients as well.

Frank E. Johnson, M.D.  
President  
Minnesota Medical Association



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## Editor's Notebook

### HMOs — A Matter of Choice

*"The HMOs in Minneapolis-St. Paul have demonstrated that a variety of health-care plans can develop, attract employers and become financially stable in a relatively short period, with little assistance from the public sector . . . There appears to be nothing in the Minneapolis-St. Paul experience that would preclude duplicating it in other areas through private actions."*

Jon Christianson, PhD, and Walter McClure, PhD  
Health Care Economists, InterStudy, Excelsior, Minnesota  
"Competition in the Delivery of Health Care",  
*New England Journal of Medicine*, Volume 30, pages 812-819, 1979

*"The physicians in Minnesota are now witnessing the widespread local and national press coverage given to Health Maintenance Organizations. It is important to recognize that the growth of these organizations is a slow one — except in Minnesota — despite the Federal government's attempts to promote more operational plans."*

Alfred Anderegg, M.D., Private Practitioner, Suburban Minneapolis,  
Chairman of Board of Physicians Health Plan, and former Medical  
Director of Group Health, "HMOs — Their Limitations and Role"  
*Minnesota Medicine*, Volume 62, pages 797-799, 1979

To hear Minneapolis-St. Paul HMO boosters talk, you would think HMOs are about to sweep through the country like a prairie fire. The spark for the fire? Competition between HMOs and between HMOs and independent fee-for-service practitioners for the health care dollar. The aftermath of the fire? Reduced health care costs because of competition and the diminished role of fee-for-service medicine. At least that's the scenario you keep hearing and reading.<sup>1-5</sup>

#### Differences between HMO Boosters and Others

Yet, when you talk to physicians and patients, you get a more cautious and colder appraisal. Why the difference? One reason, I suspect, is that most of the HMO pushers are planners, economists, and managers who view the "health care systems" organizational aspects and its rationality. To them, HMOs have great appeal because they are part of a competing voluntary system in harmony with a free market economy based on choice. Besides, HMOs, being organizations that contract with other organizations, provide a means of control that you lack when you deal with myriads of practitioners and specialists paid on a fee-for-service basis.

#### Physicians' Attitudes

Physicians feel differently: After all, they didn't go into medicine to be controlled by an organization or to be subjected to its disciplines. They are men of knowledge and



independence, capable of deciding what's best for themselves and their patients. Anyway, HMOs care for only the healthy employed segment of the population, represent a kind of self-imposed bureaucracy, and have no mechanisms for supporting research and training.

### **Patients' Feelings**

And the patients? They may be resisting flocking to HMOs simply because they are unaware of their presence. The government is trying to change this: if a federally-qualified HMO opens within 25 miles of your business and you employ 25 or more people, you *must* offer the HMO as an option to the more common Blue Cross or Blue Shield plan. This law has been in effect since 1973, but HMOs have still not caught on. Why not? Some patients dislike the lack of freedom to choose or change physicians or institutions. They are also skeptical about an organization that economizes on *their* health care. Finally, many patients seem satisfied with their current physician and the current system.

Aaron Wildavsky, President of the Russel Sage Foundation, explains the problems of HMOs this way:

“Since the basic method of cutting costs is to reduce the supply of hospital beds and physician services, HMOs work by making people wait. Since the physicians are on salary, they must be given a quota of patients or a cost objective against which to judge their efforts. Both incentives may have adverse effects on patients. HMO patients complain about the difficulty of building up a personal relationship with a doctor who can be seen quickly when the need arrives.”<sup>6</sup>

### **Slow HMO Growth**

HMOs, in short, are a mixed bag with questionable tradeoffs between efficiencies and effectiveness. Still, in a General Mills Survey, only 2 percent of HMO enrollees were dissatisfied with their choice, and 45 percent report their care was better than before.<sup>7</sup> But HMO growth remains slow, except in geographic pockets like the Twin Cities. HMOs are still growing nationally at less than five percent a year, despite heavy handed support from the government, i.e., the 1979 Amendment to the Health Planning and Resources Development Act that exempts HMOs from Certificate of Need coverage.

As of August 1978, just under 7.5 million people, less than five percent of those eligible, were participating in HMOs (Figure).

The Twin Cities, as you can see, are one of the hotbeds in the United States for HMOs. As of December 31, 1978, Twin Cities HMO enrollment totaled 240,800 members, or 12.4 percent of the population.<sup>1</sup> That percent figure is now somewhere near 20 percent, and Minneapolis and St. Paul have roughly three times more HMO enrollees per capita than the rest of the United States. This performance has emboldened Twin City-based Health Care consultants, Christianson and McClure of InterStudy, to predict HMOs will grow as fast elsewhere,<sup>1</sup> and Senator David Durenberger to introduce his Health Incentives Reform Act (S. 1968), which is based on the Twin Cities' experience and which would require employers to offer each employee a choice of at least three alternative HMO plans.

### **Proposed HMO Scenario**

As the InterStudy people and Durenberger see the scenario, it would evolve like this. After employers offer HMOs, the concept will catch on and “capture” somewhere between 20 and 40 percent of the “market”. At that point, physicians will have to compete by either forming their own open panel HMOs, i.e. IPAs (Independent Practice Associations), or by changing their fee-for-service style in such a way to compete economically. Once all physicians are compelled to join competing health plans or forced into HMO-like behavior, government regulations will be unnecessary, physicians will remain autonomous, and the cost of health care will take care of itself.



Peter Drucker describes this evolution this way:

“In health care, we may well move to a system that establishes the principle that everybody is entitled to prepaid health care — paid for either out of employees’ insurance or by government for the aged and poor. Yet, we may well encourage considerable differentiation between different kinds of health plans, and considerable competition between different kinds of health care institutions with different plans and different priorities.”<sup>8</sup>

### The Twin Cities — A Distorted Prism

Is this the way it’s going to be? I’m dubious, because I think the Twin Cities is a distorted prism through which to view HMO events. Since 1971, HMOs enrollments have grown at a rate of 27 percent here, doubling every three years. There are already signs that growth is slacking off. For example, Group Health’s current WCCO advertising campaign may well

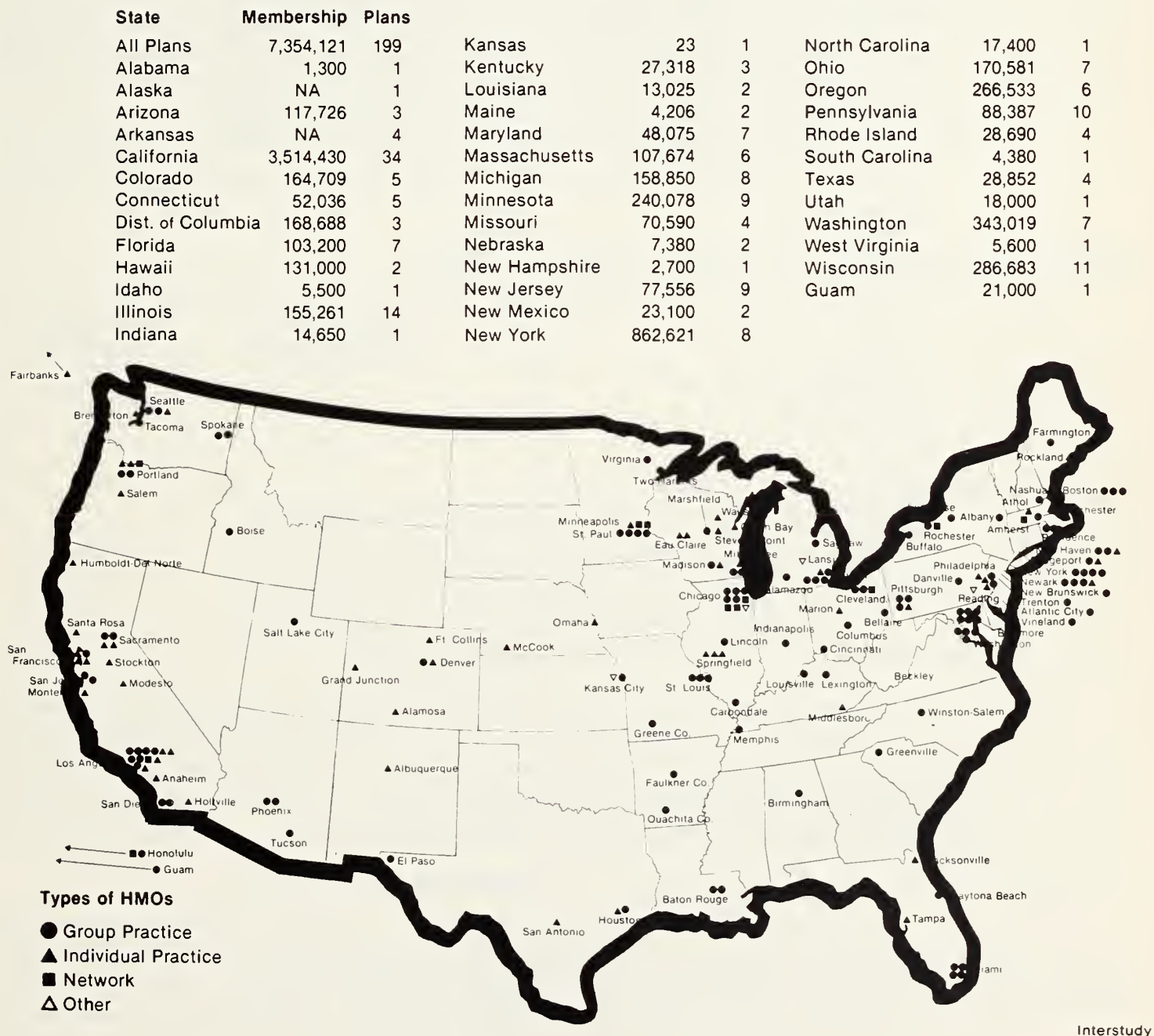


Figure — HMOs as of August 1978, reproduced by permission from a Kaiser Medical Foundation publication “Organizing Health Care Delivery Systems: A Historical Perspective.” HMOs shown here are of two basic types: the group prepayment type and the Individual Practice Association (IPA).



be because its growth rate has slowed. Nonetheless, we are being widely touted as a “model” for the rest of the country. But are we like the rest of the country? I don’t think so.

### A Cauldron of Experimentation

We just happen to be a cauldron for health care experimentation because we have the right mix of ingredients. These include: (1) a tradition of group practice — five times the national average; (2) a large number of medical school graduates (340 a year from Minnesota schools) with a resulting crowding and competition between physicians; (3) a “progressive” political tradition that fosters various forms of collectivism; (4) a high proportion of citizens with hospitalization insurance; (5) a low proportion of minorities; (6) a well-educated populace with a high employment rate; (7) the existence of three or more established competing plans; (8) a sophisticated marketing environment in which providers, consumers, and employers are well-informed; (9) an unusually large number of articulate HMO spokesmen — Paul Ellwood and his InterStudy Group, Medical Directors for existing HMOs, and, more recently, Senator David Durenberger; (10) an open-minded medical profession that doesn’t fear new ideas; and (11) a heavy concentration of major corporations who are anxious to reduce the uncertainties of health care escalation.

A note about the last point. Minneapolis-St. Paul is the home of 22 billion dollar corporations. Compare this to the number of corporations in entire states (Table), and you get the picture.

TABLE  
Concentration of Billion Dollar Corporations in Twin Cities Compared to Entire States.

Location	Population	Number of Billion Dollar Corporations	Corporations/million people
Minneapolis-St. Paul	2.0	22	11.0
Connecticut	3.8	29	7.6
New York State	18.3	123	6.7
Illinois	11.2	55	4.9
Ohio	10.7	41	3.8
Michigan	8.9	22	4.0
Pennsylvania	11.8	36	3.3
Missouri	4.7	14	3.0
New Jersey	7.2	21	2.9
Texas	11.2	27	2.4
California	20.0	52	1.8

### The Right Mix

Minnesota, in other words, has the right mix of physicians, people, managers, planners, and businessmen to make HMOs go. Similar mixes exist in a few other places — Wisconsin, the California Cities, Portland and Seattle, and Washington, D.C. and maybe a few other metropolitan areas — but not many. Note in the Figure that 13 states have no HMOs at all. Rural HMOs, except in Minnesota and Wisconsin are practically nonexistent.

### HMO Failures

Also keep in mind that many HMOs have failed — in Brooklyn, Phoenix, Baltimore, and most recently, in Fort Collins, Colorado. Some of these failures have taught painful lessons. For example, spokesmen for the John Hopkins HMO in Columbia, Maryland, learned these hard lessons: (1) An HMO requires a large population base; (2) a great deal of start-up capital is required; (3) government regional planning may confuse and slow HMO efforts; (4) physicians must be given monetary and decision-making incentives; (5) marketing is difficult and complex and must have access to uncommitted industrial groups; (6) the benefit package must not be too broad and should be accompanied by relatively high co-payments; (7) the patient must understand and participate in the process; (8) antagonism



by county and state medical societies can be distracting and even fatal; and (9) incomes for physicians, especially specialists, is high and can strain the HMO budget.<sup>9</sup> The Johns Hopkins' people conclude that setting up an HMO is difficult at best and requires ability to market to large groups, strong medical leadership, control mechanisms, and a reasonable, i.e. not too broad, benefit package.

### A Matter of Choice

Are HMOs the wave of the future? Maybe. But the tide has grown slowly and may have already crested. HMOs have only worked well with limited populations of relatively healthy people. As a rule these healthy people have not included the aged, the infirmed, the mentally ill, or the psychologically crippled. Most HMOs composed of Medicaid patients have failed, and most HMOs, with the exception of those in the Twin Cities, have required government money to get started.

Physicians and businessmen, for understandable reasons, are uneasy about organizations that require government subsidies to survive. HMOs will probably only grow to the extent which the government imposes. There is a fundamental question whether centralized organizations, such as HMOs, can prosper in a decentralized country like the United States. In any event patients should be free to choose between HMOs and their own physicians rather than by being compelled to join "consumer-choice" health plans.



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RICHARD B. TOMPKINS, MODERATOR

7:30 Arthritis - History and Physical Examination (Roger S. Colton)  
8:25 Cutaneous Clues to Rheumatic Diseases (Harvinder S. Luthra)  
9:20 Break  
9:40 Differential Diagnosis and Treatment of Raynaud's Phenomenon (Richard B. Tompkins)  
10:35 Differential Diagnosis of Polyarticular Arthritis (Conrad S. Butwinick)  
11:30 Adjournment

FRIDAY, FEBRUARY 22, 1980

HARVINDER S. LUTHRA, MODERATOR

7:30 X-rays in Diagnosis of Rheumatic Disease (John W. Worthington)  
8:25 CBC, ESR, C-Reactive Proteins (Conrad S. Butwinick)  
9:20 Break  
9:40 Antinuclear Antibodies and Extractable Nuclear Antigens (Roger S. Colton)  
10:35 HLA and Complement in Rheumatic Diseases (Harvinder S. Luthra)  
11:30 Adjournment

SATURDAY, FEBRUARY 23, 1980

JOHN W. WORTHINGTON, MODERATOR

7:30 Structure, Biochemistry and Metabolism of Articular Cartilage (John W. Worthington)  
8:25 Pathophysiology of Osteoarthritis (Harvinder S. Luthra)  
9:20 Break  
9:40 Systemic Lupus Erythematosus and Mixed Connective Tissue Disease (Conrad S. Butwinick)  
10:35 Purine Metabolism (Richard B. Tompkins)  
11:30 Adjournment

MONDAY, FEBRUARY 25, 1980

ROGER S. COLTON, MODERATOR

7:30 Immune Complexes and Disease (Harvinder S. Luthra)  
8:25 Pathophysiology of Rheumatoid Arthritis (Richard B. Tompkins)  
9:20 Break  
9:40 Physical Medicine in Treatment of Rheumatic Diseases (Roger S. Colton)  
10:35 Surgery in Rheumatic Diseases (John W. Worthington)  
11:30 Adjournment

TUESDAY, FEBRUARY 26, 1980

CONRAD S. BUTWINICK, MODERATOR

7:30 Aspirin and Nonsteroidal Anti-inflammatory Drugs (Conrad S. Butwinick)  
8:25 Corticosteroids and Immunosuppressives in Treatment of Rheumatic Diseases (Roger S. Colton)  
9:20 Break  
9:40 Gold, Penicillamine and Levamisol (John W. Worthington)  
10:35 Treatment of Gout and Hyperuricemia (Richard B. Tompkins)  
11:30 Adjournment

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# Duodenal Rupture after Blunt Abdominal Trauma

ROBERT R. M. GIFFORD, SR. M.D.\*† and ALAN C. HYMES, M.D.\*

Following blunt abdominal trauma from a steering wheel in an automobile accident, a 56 year-old woman complained of abdominal pain and nausea. Twenty-three hours after the accident, diagnosis of traumatic duodenal injury was made. Post-operatively, she had a brief episode of pancreatitis, but recovered, and was discharged on the tenth post-op day.

**D**UODENAL INJURY is an uncommon sequel to blunt abdominal trauma in auto accidents. Usually, the steering wheel provides the injury. A delay in diagnosis is a reflection of the non-specific physical findings of retroperitoneal hollow viscus injury and its attendant subtle roentgenographic changes. Successful management is predicated on early diagnosis and prompt surgery.

Most blunt duodenal injuries involve the second, third and fourth portions while the first, post-pyloric, segment is infrequently damaged. We wish to report such a first portion duodenal injury sustained in an auto accident.

## Case Report

A 56-year-old woman was in an auto accident on the night of admission. Her car was struck from the side by another auto, with both vehicles traveling 30-40 m.p.h. She was not wearing a seat belt. She recalled that she was thrown forward, hitting her forehead on the windshield, her trunk against the steering wheel and her knees against the dashboard.

Her vital signs were stable with a temperature of 99.2°F. She complained of nausea, abdominal pain and pain in her knees and forehead which were abraded. She had an 8 x 8 cm. bruise just to the right of her umbilicus. Bowel sounds were hypoactive. Her abdomen was tender but showed no guarding or rebound. Laboratory data included hemoglobin of 14.2 gm. %, WBC of 7700 cells/mm<sup>3</sup>, negative urinalysis, and serum amylase of 182 IU/L. Roentgenograms of the skull, knees, abdomen and chest were negative.

She was admitted because of her abdominal pain and nausea. The following morning (12 hours post-injury) she had the same symptoms and findings. Late that afternoon her nausea worsened to the point of vomiting, associated with a decrease in bowel sounds and severe abdominal distension. Her tenderness began to localize to the right abdomen. Repeat WBC was increased to 11,000 cells/mm<sup>3</sup> with hemoglobin 14 gm. % and serum amylase increasing to 387 IU/L. Urine amylase was 1800 IU/hr. Naso-gastric suction was

begun, producing normal gastric contents and no blood. Repeat abdominal roentgenograms (Figures 1(A) and (B)) revealed a honey-combed air pattern in the right upper quadrant, and on the decubitus film free air outlined the right colon wall. Gastrografin instillation through the naso-gastric tube revealed leakage of contrast from the first part of the duodenum into the sub-hepatic and retroperitoneal space. The diagnosis of traumatic duodenal injury was made 23 hours post-injury.

At operation there was a 2 cm. longitudinal tear of the first portion of the duodenum, in the intraperitoneal segment (Figure 2),

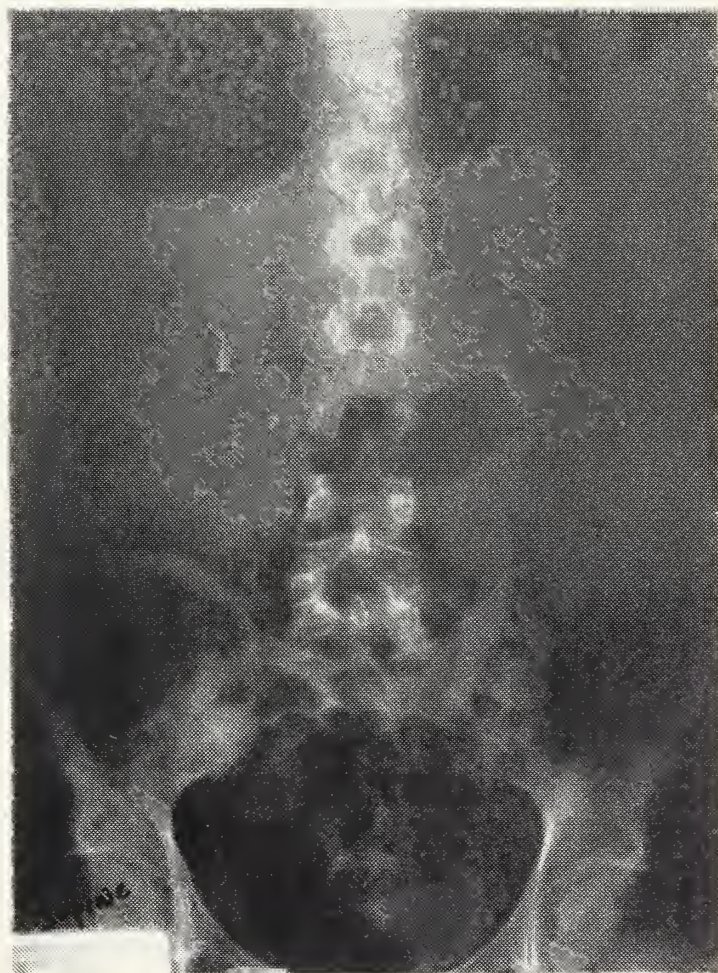


Fig. 1 (A) — Roentgenogram taken approximately eighteen hours post-injury demonstrates, on the supine view honey-combed air pattern in the right upper quadrant beneath the hepatic shadow.

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Fig. 1 (B) — Roentgenogram taken approximately eighteen hours post-injury demonstrates on the left lateral decubitus view free peritoneal air outlining the right colon wall.

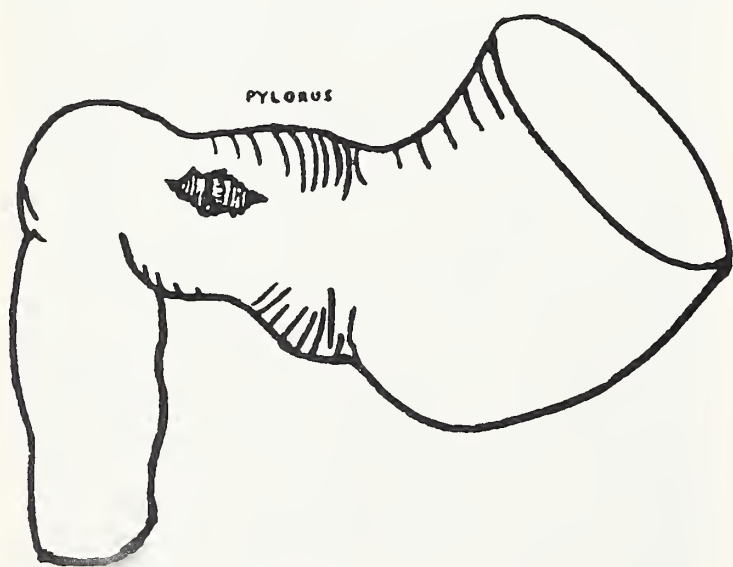


Fig. 2 — Sketch of operative findings shows longitudinal tear, approximately 2 cm. in length, in intra-peritoneal first portion of duodenum.

approximately 4-5 cm. from the pylorus. The serosal tear was linear without associated serosal contusion. The duodenal mucosa was clearly lacerated without a submucosal hematoma. The liver edge had dropped to seal the hole, causing duodenal contents to collect in the subhepatic space and dissect retroperitoneally. There was no other apparent intra-abdominal injury.

The duodenal laceration was closed in two layers using chromic for the mucosa and Tevdek for the serosa. A piece of omentum was then tacked over the closure. The subhepatic and retroperitoneal space was copiously irrigated with normal saline alternating with Neomycin 0.25% solution. No drains were placed.

Post-operatively she had a two or three day episode of mild pancreatitis and was discharged on her tenth post-operative day. 14 months later she remains well.

### Comments

In several clinical series of blunt duodenal injuries, involvement of the first duodenal portion is infrequent, ranging from 0-8%.<sup>1-11</sup> In view of how infrequently blunt duodenal injuries occur, this reported case is even more uncommon as an isolated injury.

In patients, with blunt abdominal trauma, duodenal injury must always be suspected. Physical findings are non-specific unless peritonitis is present. There is usually abdominal wall tenderness and possibly an ecchymotic area. Since most duodenal injuries are retroperitoneal, findings are few until persistence or progression of symptoms strongly suggest significant injury.

Laboratory data may also be initially equivocal. Talbot and Shuck<sup>2</sup> found that 50% of patients had normal initial roentgenograms and 60% had a normal serum amylase. Peritoneal aspiration was negative in 75% of cases.

Aside from clearly positive roentgenograms or positive peritoneal aspirate/lavage, the most influencing factor prompting surgery was peritoneal irritation.<sup>1-3</sup> The average time from injury to operation varied widely from immediate to several days. Apparently, the critical prognostic period is the first 24 hours, for those explored during this time had a mortality of 5-11% whereas there was a 40-65% mortality in those explored after 24 hours.<sup>1-8</sup>

The extent of duodenal injury varies from an intra-mucosal hematoma or non-penetrating laceration (19%), to perforation or laceration of duodenum (59%), to pancreatoduodenal disruption (22%).<sup>4</sup> Most blunt duodenal ruptures are transverse, retroperitoneal and in the second, third or fourth portions of the duodenum.<sup>3,5,8</sup> The case reported here is remarkable in that the injury was in the first portion of the duodenum and the tear was longitudinal rather than transverse which is the usual finding.



Operative management is dictated by the type of the duodenal injury and associated pancreatic or biliary involvement. Debridement and suture of the defect with drainage is most commonly employed. Omission of drainage did not increase the complications. Additional omentum or jejunal serosal patching has been used. For more involved injuries not amenable to direct suture, resection with duodeno-duodenostomy or duodeno-jejunostomy may be performed. For more severe injuries of the duodenum, such as transection associated with pancreatic injury, or biliary tract disruption, by-pass procedures are used, and if necessary, pancreatoduodenectomy, carrying with it a mortality as high as 73%.<sup>9</sup>

The complication rate is related to the length of delay to operation, extent of duodenal injury and presence or absence of pancreatic involvement. Duodenal or pancreatic fistula occurred in 6-30% of patients, but no fistula developed when an operation was done within the first 24 hours.<sup>1,3,4</sup> Subphrenic, subhepatic or other abdominal abscess, pancreatitis or bowel obstruction occurred in 6-18%. For those

duodenal injuries with concomitant injury to other viscera, morbidity and mortality increased proportionately.

Several mechanisms have been proposed for traumatic duodenal injuries. Webb, et. al., suggested that the closed duodenal loop bordered by the pylorus and the acute angle of the ligament of Treitz, is suddenly compressed by the abdominal trauma and ruptures.<sup>10</sup> This would explain most second and third portion duodenal injuries. Injuries to the fourth portion of the duodenum result from direct trauma forcing the duodenum against the vertebral column.<sup>3,5</sup> Fish and Johnson suggested another mechanism in which the abrupt compression of the rib cage with upward displacement of the liver, can tear the duodenum by traction of the hepato-duodenal ligament.<sup>11</sup> However, these mechanisms fail to explain first portion duodenal injuries. Bergquist and Hedelin state that intraperitoneal duodenal injuries result from a combination of mechanisms: a bursting closed loop, a tangential shearing force and a tear by the hepato-duodenal ligament.<sup>5</sup>

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# Varicella Immunity in Adults

KARL E. GROTH, B.S.\*; JEFFREY McCULLOUGH, M.D.\* and HENRY H. BALFOUR, JR., M.D.\*

Two hundred consecutive blood donors were studied for immunity to varicella. Histories were positive in 65%, complement-fixing (CF) titers in 69%, and indirect immunofluorescent (IF) titers in 97.5%. We concluded that history was an unreliable indicator of varicella immunity, and that the CF testing was relatively insensitive. Adult exposures in our area are unlikely to result in varicella because most adults (97.5%) are immune. Varicella can produce congenital malformations or acute neonatal disease, however, and we recommend that exposed pregnant women with a negative history be tested for antibodies to varicella-zoster virus. Those lacking IF titers should be given zoster immune plasma or globulin. Because zoster immune plasma is in constant demand, we suggest that shingles patients be asked to consider donating blood.

**V**ARICELLA (CHICKENPOX) is a mild disease in normal children, but can be severe in immunocompromised patients<sup>1</sup> and neonates,<sup>2</sup> and may result in pneumonia in adults.<sup>3</sup> Because physicians frequently are consulted by concerned adults who do not have a history of varicella and have been exposed, we studied 200 blood donors to determine the actual proportion of varicella-susceptible adults in our area.

## Materials and Methods

Histories of varicella or zoster were taken from 200 consecutive healthy adults who came to the University of Minnesota Health Sciences Center for routine blood donation during January and February 1976. Venous blood was drawn aseptically, sera separated from the clot at room temperature, and the samples stored at  $-70^{\circ}\text{C}$  until tested. Sera were assayed for varicella-zoster virus (VZV) complement-fixing (CF) antibody in a microtiter system using 4 units of antigen (obtained from Microbiological Associates, Bethesda, MD) and two exact units of complement. Serial twofold dilutions of serum were tested and titers expressed as reciprocals of the highest dilution showing complete fixation of complement after 18 hours incubation at  $4^{\circ}\text{C}$ . Sera were also tested for indirect immunofluorescent (IF) antibody to VZV using a modification of the membrane fluorescence method of Williams et al.<sup>4</sup>

Serum dilutions of two, four, and eight were tested for IF antibodies. Donors were considered susceptible to varicella if their VZV CF titers were  $<4$  and their IF titers  $<8$ . This study was approved by the University of Minnesota Committee on the Use of Human Subjects in Research, and informed consent was obtained from the subjects before participation.

## Results

The participants were between 17 and 66 years of age (mean age, 29.9 years; median age, 30 years). Correlation of history of varicella with serologic immunity is shown in Table 1. Of the 200 donors, 130 (65%) had positive histories of varicella and two (1%) of zoster. History was a less sensitive indicator of immunity than antibody testing. By the CF antibody method, 138 (69%) were immune, and by the IF technique 195 (97.5%) had evidence of immunity. Furthermore, histories appeared to be erroneous: three subjects who gave a positive history lacked both IF and CF antibodies to VZV. In contrast, 26 (93%) of those

TABLE 1  
Comparison of History and Serologic Tests as  
Indicators of Immunity to Varicella

Method	Positive	Negative	Uncertain
History	130 (65%)	28 (14%)	42 (21%)
Complement- fixing antibody test	138 (69%)	62 (31%)	—
Immuno- fluorescent antibody test	195 (97.5%)	5 (2.5%)	—

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with a negative history had positive IF titers. The distribution of CF antibody titers in our blood donor population is shown in the Figure. Ten (5%) of the donors had CF titers  $\geq 32$ , although they did not have a recent history of either varicella or zoster. The distribution of CF titers by age of donor is shown in Table 2. No significant age-related differences were found either in the geometric mean of the groups or the distribution of titers. The lowest geometric mean titer and the highest proportion of subjects with titers  $<4$  were in the 31-40 age group, but the differences were not statistically significant compared to other age groups. The five donors who were seronegative by both CF and IF tests were 18 to 24 years old (mean age, 20 years). All subjects with IF antibodies had titers  $\geq 8$ . The five who lacked IF antibodies had titers  $<2$ .

### Discussion

The most important finding of this investigation was the fact that 97.5% of 200 normal adult blood donors in the Minneapolis-St. Paul metropolitan area were found to be immune to varicella by a sensitive IF antibody test. History of varicella was less accurate than antibody methods in predicting immune status. Histories of varicella were positive in 65%, CF titers in 69%, and IF antibody titers in 97.5%. Positive histories also appeared in error, since three donors who lacked both CF and IF antibodies gave a history of chickenpox. The CF test was much less sensitive than the IF method. Sixty-two (31%) of our donors had CF titers  $<4$  and would have been considered susceptible to varicella if that had been the only method employed. Of these 62, 57 (92%) had IF antibodies and most likely were immune to chickenpox.

Prevalence of varicella antibodies may vary geographically and one cannot necessarily extrapolate our results to other areas. Nevertheless, chickenpox is a universal infectious disease of childhood, and it is probable that for most urban populations in the United States immunity among adults is similar to that found in Minneapolis-St. Paul. Because varicella is a mild disease in normal children, the disease is quickly forgotten and a positive history underestimates the

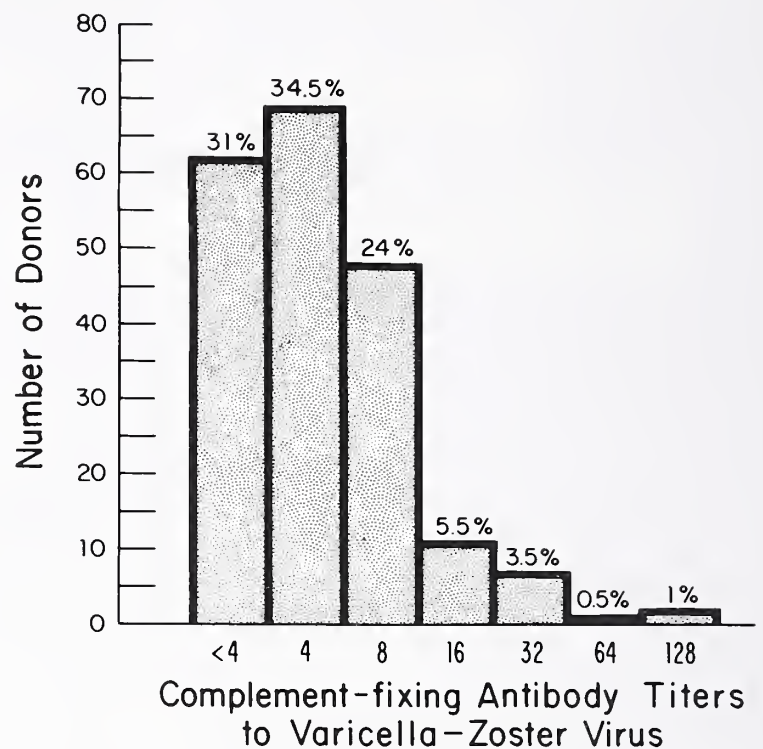


Figure — Distribution of varicella-zoster virus complement-fixing antibody titers among 200 normal adult blood donors from the Minneapolis-St. Paul metropolitan area.

proportion of adults actually immune.

Tomlinson and MacCallum reported that the prevalence of VZV CF antibody was lowest for their blood donors in the age groups of 41-50 and 51-60 years.<sup>5</sup> This supported Hope-Simpson's view that zoster results when "antibody has declined below the critical value".<sup>6</sup> Our data are not consistent with that hypothesis. The attack rate of zoster has been shown to increase steadily with increasing age,<sup>6</sup> but our donors' geometric mean antibody titers are essentially the same for all age groups tested. Likely virus-specific cell-mediated immunity is as important or more so than humoral antibody in containing latent VZV.

Does serologic immunity mean protection from clinical varicella? The most sensitive test at present appears to be the IF antibody method. The IF titers have been shown to be protective in two small hospital outbreaks of varicella.<sup>7</sup> We have tested approximately 200 normal subjects exposed to varicella and found that IF antibody has always been protective. However, two of our immunocompromised patients developed

**TABLE 2**  
Distribution of Varicella-Zoster Virus Complement-Fixing Antibody Titers by Age

Age Group (in years)	Subjects Tested	Geometric Mean Titer	No. of subjects with CF titers of						
			<4	4	8	16	32	64	128
17-20	25	3.7	8	9	6	1	0	0	1
21-30	107	4.0	29	40	25	8	3	1	1
31-40	38	3.0	17	9	8	1	3	0	0
41-50	19	3.9	4	9	5	1	0	0	0
51-66	11	3.8	4	2	4	0	1	0	0



varicella despite positive IF titers. One was a child with acute lymphoblastic leukemia and the other a renal allograft recipient. Both children had negative histories of chickenpox and lacked CF antibody. The CF test is less sensitive than the IF method but may be a better predictor of immunity in immunocompromised patients. In our experience no patient, normal or immunocompromised, with CF antibody has ever developed chickenpox. In summary, we are confident that normal adults with positive titers (CF or IF) are immune to varicella. However, immunocompromised patients may not be and we recommend zoster immune plasma (ZIP) or zoster immune globulin (ZIG) prophylaxis unless such patients have *both* a history of varicella and positive IF antibody titers.

Should normal adults "susceptible" to varicella be given ZIP or ZIG to attempt to modify chickenpox? We would say "no" for the following reasons: (1) The vast majority of adults are immune despite a negative history. (2) Most normal adults (probably more than 99%) will have relatively mild chickenpox. Varicella pneumonia is more common in adults than children but is usually not severe and is very rarely fatal.<sup>3</sup> (3) The shortage of ZIP or ZIG prompts conservation of the material for immunocompromised patients who are at high risk for severe varicella infection.

Varicella exposures in pregnant women, which often cause alarm, rarely result in clinical disease because most women are protected by previous infection. However, congenital malformations due to varicella early in pregnancy have been described.<sup>8</sup> Chickenpox also is a risk to the neonate if a susceptible pregnant woman develops the disease during the period from one week before to the week after delivery.<sup>2</sup> Because of this, women who are exposed to chickenpox and whose history of varicella is negative

or uncertain should have a VZV IF antibody test. Those who lack IF titers should be given ZIP or ZIG as soon as possible after exposure.

Since varicella can be severe and even fatal in immunocompromised hosts, we are in constant need of plasma donors convalescent from zoster. Plasma or globulin prepared from these donors can prevent or modify varicella and there is a suggestion that higher titered material is more effective.<sup>9-11</sup> We have established 32 as the minimum acceptable CF titer for ZIP.<sup>9</sup> Recently, Zaia and his coworkers in Massachusetts prepared varicella-zoster immune globulin from random blood donors.<sup>12</sup> They found that 97 (7.4%) of 1313 donors had CF titers  $\geq 32$ . Their data are similar to ours: 10 (5%) of 200 Minnesota blood donors had CF titers  $\geq 32$ . Thus, it is possible to find random donors with adequate VZV titers for preparation of ZIP or ZIG. At the present time, however, we prefer to use plasma donors who are convalescent from zoster. We have shown prophylactic efficacy for this material,<sup>9,10</sup> whereas the usefulness of globulin prepared from random donors has yet to be conclusively demonstrated. If plasma or globulin prepared from random donors proves to be effective in preventing or modifying varicella, the supply of hyperimmune material would be greatly enhanced. Then, we might consider its use in normal susceptible adults exposed to varicella.

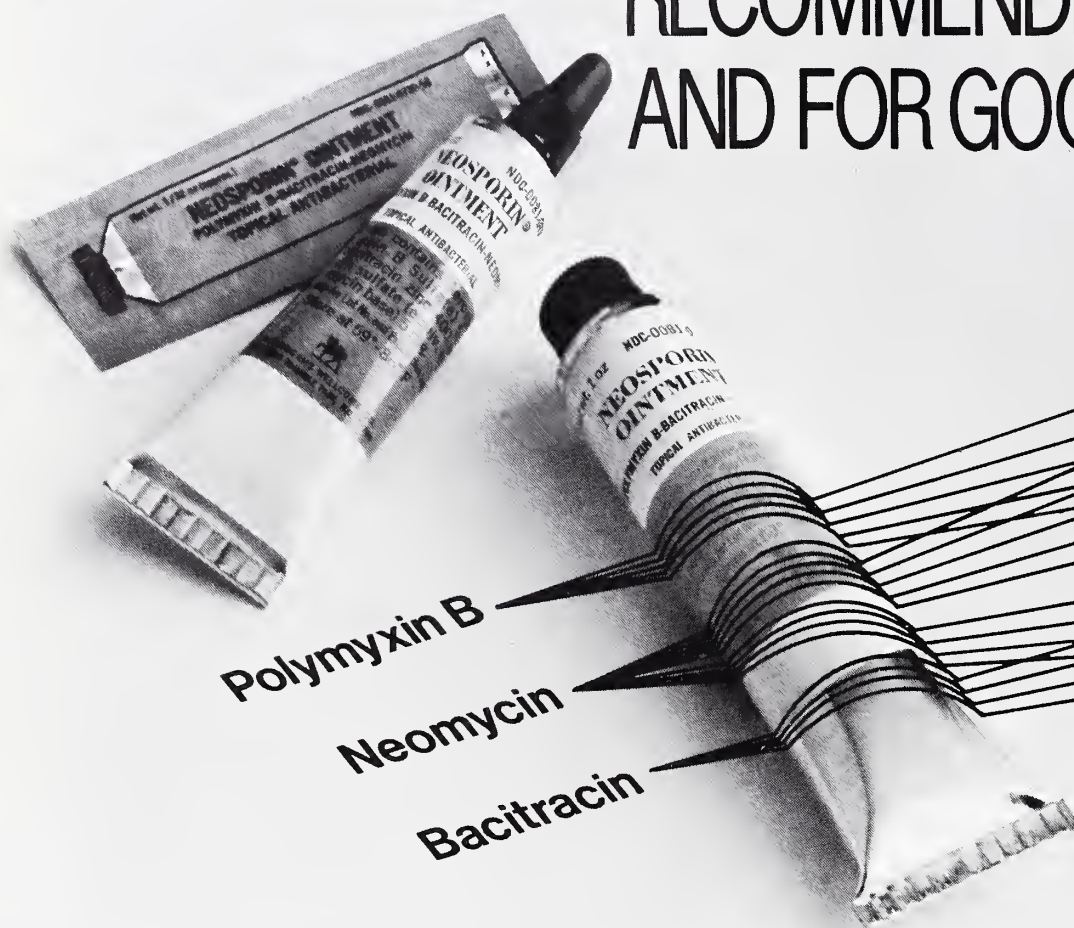
In closing, we urge physicians to remind patients with shingles that their plasma is in demand and may be life-saving for immunocompromised patients. Until varicella vaccine becomes widely available, there will be a continuous need for ZIP or ZIG to prevent varicella in exposed, susceptible immunocompromised patients and exposed, seronegative pregnant women.

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# Indochinese Refugees

## Health Screening of Indochinese Refugees

GEORGE R. PETTERSEN, M.D., M.P.H.;\* ARTHUR E. NOOT;† ANDREW G. DEAN, M.D., M.P.H.#  
and MICHAEL OSTERHOLM, PH.D., M.P.H.§

Medical screening of Indochinese refugees is important to insure health for the individual and to prevent disease transmission. Screening, treatment, or immunization received in Asia should not be assumed complete unless well-documented.

The following health services should be provided to each newly arrived refugee:

- a. General evaluation and treatment for acute medical problems, including those related to nutrition.
- b. A visual inspection of the refugee for evidence of significant skin conditions.
- c. Immunization as appropriate to begin, continue, or complete recommended schedules.
- d. Any procedures, such as further evaluation for tuberculosis indicated by results of tests done in Asia.
- e. Full documentation of all procedures, findings and treatments.
- f. Assured referral to an identified, appropriate source of continuing health care (including mental and dental care, if indicated) with accompanying appropriate records. A wallet sized medical record card is available from the Indochinese Resettlement Office (Phone number below). (See last page.)
- g. Testing for hepatitis B surface antigen (HBsAg) before dental care is begun or if the patient is pregnant or entering a hospital.
- h. An evaluation for significant parasitic diseases and infestations with appropriate treatment as necessary.

Questions should be directed to the Division of Disease Prevention and Control (612) 296-5414, or Sandra Du Vander, Indochinese Resettlement Office, Department of Public Welfare (612) 297-2777, or MMA office 222-5431.

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## Screening of Southeast Asian Refugees

Agencies sponsoring refugee immigration estimate that 3,000 refugees from Southeast Asia may arrive in Minnesota during the next 12 months. Federal authorities state that the medical screening provided prior to the arrival of these refugees in the U.S. is frequently inadequate.<sup>1</sup> Many have not received recommended immunizations. The regional office of the Department of Health, Education and Welfare suggests that local public health authorities assure that each newly arrived refugee receive medical screening.

The following recommendations are provided for physicians caring for newly arrived SE Asians. These recommendations are intended to supplement the general medical examination for clinically apparent problems, such as malnutrition or anemia, which are commonly found in this group.

1. Tuberculosis: (Twenty-six cases were found among SE Asians in Minnesota in 1978.) We suggest the following screening procedure if the patient has not previously been screened by a facility of known reliability: (1) Persons through age 21 should be skin tested using needle, syringe and PPD. (2) Persons over 21 should receive both a skin test and a chest x-ray.

A skin test reaction of 10 mm or more of induration, regardless of BCG status, should be considered a true positive for purposes of prophylactic treatment. Positive skin test reactors through age 21 should receive a chest x-ray, and other evaluation as needed, to rule out active disease. Persons through age 21 infected without disease should receive one year of preventive therapy. All persons with active disease should receive at least 12-18 months of therapy, with at least two drugs, chosen with the aid of drug susceptibility tests. Smear positive cases should be treated with three drugs.

2. Immunization: Physicians should not assume that this has been accomplished. Active steps, including follow-up, should be taken to insure that children have received a full series for measles, rubella, mumps, pertussis (under age 6), diphtheria, tetanus and polio. Adults should receive tetanus and diphtheria toxoid.



3. Intestinal parasites: Detected by stool examination. *Ascaris* should be treated, and hookworm and *Trichuris* should be treated if large numbers of eggs are present. Mebendazole (Vermox) may be used to treat all three (plus pinworms) if the patient is not pregnant. *Giardia* may be treated with one of three drugs — quinacrine hydrochloride (Atabrine), metronidazole (Flagyl) or fluorazolidone (Fluroxone), but all three have disadvantages. A recent review article suggests quinacrine hydrochloride for *Giardia* in adults, and fluorazolidone for children<sup>2</sup>. Some parasites, including *Clonorchis sinensis*, should not be treated unless symptoms are present. Consultation on recommended treatment for other parasites is available through the Acute Disease Epidemiology Unit at 612/296-5414.
  4. Malaria and venereal disease: There have been very few clinical cases of malaria, syphilis or gonorrhea reported in Minnesota's SE Asian population. Screening for these conditions is of secondary importance unless clinically suspected.
- NOTE: Several cases of malaria have occurred recently (December '79). Malaria screening is suggested in groups or families known to have had cases and in any case of fever.
5. Leprosy: Rare. We are aware of only one case residing in Minnesota. The disease is detected by inspection of the skin. Macular depigmented lesions, particularly if anesthetic to pinprick, or nodules along the course of major peripheral nerves should suggest further work-up.

### **Viral Hepatitis, Type B Testing for Indochinese Refugees?**

Preliminary data from the screening of Indochinese refugees entering Canada indicate that about 12% of them are positive for hepatitis B surface antigen (HBsAg)<sup>3</sup>. Most of these individuals are chronic, asymptomatic carriers of the antigen.

Hepatitis B virus (HBV) is found in blood and serous body fluids. Transmission is also possible via saliva and semen, but the relative efficiency of such transmission has not yet been determined. Most transmission is thought to occur when infective fluids enter the body of a susceptible person through a break in the skin, or penetrate through a mucous membrane or the eye<sup>4</sup>. Body fluids containing HbsAg can contaminate environmental surfaces, but there is no

evidence that the virus can withstand routine cleaning, disinfection or sterilization.

Transmission to school-age contacts of carrier children or work contacts of adult carriers is not likely to occur under normal hygienic conditions. Nor is transmission likely to occur when carriers are employed as foodhandlers or as hospital personnel, or from use of swimming pools, toilet facilities, drinking fountains, restaurants or other public facilities.

However, there is a higher likelihood of transmission to neonates (during childbirth), to certain health facility personnel, and to those families sponsoring orphans or refugee families with young children. While perinatal transmission and resultant chronic carriage is unusual in European and American populations, it has been found more frequently in Asian populations<sup>5</sup>. The neonate may be infected during delivery, and subsequently become a carrier of HBsAg.

Little is known about the experience of adopted Indochinese refugees, but the available data suggest that there is an increased risk of transmission to families adopting small children who are HBsAg positive<sup>6,7</sup>. It is not clear how this risk applies to families who are hosting carrier children for a short time.

The Center for Disease Control has recommended that HBsAg testing be done for all Indochinese refugees arriving in the U.S. Screening of otherwise healthy refugees for HBsAg will be of benefit only if records of the test results are readily accessible when a patient seeks medical care, or if the patient informs dentists and laboratory technicians of his carrier state. In most cases, the latter would demand a level of understanding which can scarcely be expected of someone still struggling with a new language.

Certain persons and groups, particularly those involved in health care, are at a greater risk of acquiring hepatitis B than the general population because of occupational and environmental exposures<sup>8</sup>. In hospitals, proper handling of blood and other body fluids of HBsAg carriers by hospital personnel is necessary. Screening of hospitalized Indochinese is advisable, since immune globulin prophylaxis is warranted for "HBsAg-positive needle stick" exposure of hospital personnel. Dental personnel and oral surgeons are at some risk because they frequently sustain trauma to their hands while in contact with potentially infectious blood or saliva, which may also come in contact with their eyes and mucous membranes. To prevent possible exposure, dental personnel should wear gloves, face masks and eyeglasses when



treating HBsAg carriers.

It is important to determine the HBsAg status of pregnant refugee women. The risk of transmission to the infant is diminished by preventive efforts at delivery. After being thoroughly bathed, the neonate of a carrier mother should receive hepatitis B immune globulin (HBIG) — or immune globulin (IG) if HBIG

is not available — as soon as possible after birth, and certainly within 48 hours. Various dosages have been recommended<sup>9,10</sup>.

Screening for HBsAg may also be helpful to families adopting HBsAg-positive Indochinese children, or teachers in daycare centers with young refugee children.

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## Indochinese Refugee Medical Cards

Health screening procedures for the Indochinese refugees have undergone considerable changes as we learn more about their health needs. Because of language barriers, one difficult problem has been knowing what tests have already been given. The Minnesota Medical Association's Ad Hoc Committee on Indochinese Refugees has developed a wallet sized card to be carried by the refugee when seeking medical care. The front side uses a check-off system for health problems relating to present illness (PI), past history (PH), and systems review (SR) with space available for immunizations received and TB test results. To better ensure continuity of care, primary examiner's name and subsequent examiners should be indicated on the card, thus providing the provider with information on previous medical problems and test results. The back side of the card provides room for significant health-related problems (Health Record) and medications given. All refugees should receive the medical card at the initial health examination. Some may have already received the card from their sponsor. Cards may be ordered from the Minnesota Medical Association office, 101 E. 5th St., St. Paul 55101, at no charge.

Note: Physicians may see the refugees for only episodic care before they move to another area.

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# Pathologic Anatomy

## Non-Hodgkin's Lymphoma with Features of "Sternberg's Sarcoma" Manifesting as a Pelvic Mass

MARK R. WICK, M.D. \* and GENE P. SIEGAL, M.D.†

**Lymphoblastic lymphoma ("Sternberg's sarcoma") is a distinctive neoplasm affecting young individuals, usually males. This disorder is of T lymphocyte precursor origin, and has characteristic histopathologic and immunohistochemical features. Though it is commonly thought to invariably present as a mediastinal mass, as many as 50 % of patients have localized tumor masses in other anatomic locations when the disease first manifests itself. We present a case of lymphoblastic lymphoma in the form of a pelvic mass in a sixteen year old patient.**

IN RECENT YEARS, advances in fine morphologic and immunohistochemical characterization of the malignant lymphomas have allowed for a more meaningful classification of these diseases. In particular, the determination of their origin in T or B cell lymphocyte lines has proved to be insightful.

In 1916 Sternberg described the syndrome of an "undifferentiated" non-Hodgkin's lymphoma in young males with mediastinal masses.<sup>1</sup> He observed that almost universally, lymphatic leukemia occurred before death in these patients. More currently, research on this clinical entity ("Sternberg's sarcoma") has established a T cell origin for the neoplastic lymphocytes in the syndrome, and emphasis on the blastic cellular morphology has led to the generally accepted designation of "lymphoblastic lymphoma (LL)."<sup>2,3,4</sup>

In their treatise on this entity, Nathwani, et al. delineated the clinical and histopathological features of LL.<sup>5</sup> One pertinent feature was that only 50% of their patients with LL had mediastinal masses. We present a case in which this disorder manifested itself as a pelvic tumor, in the absence of a mediastinal mass.

### Case Report

A 16-year-old white male noted the onset of intermittent, dull, aching rectal pain early in April, 1978. Shortly afterwards, he became constipated and had mild hematochezia. His local physician diagnosed "hemorrhoids" and prescribed steroid cream suppositories and sitz baths.

These measures gave the patient no relief, and subsequently, nausea accompanied worsening proctalgia. He was seen at a local hospital, where a pararectal mass was palpated. Proctosigmoidoscopy disclosed no intrinsic colonic pathology. A transrectal biopsy of the mass was performed, reportedly showing a "neurogenic

tumor." The patient was referred to the Mayo Clinic.

Physical examination revealed a well-developed adolescent male with normal vital signs. The only abnormal physical findings were diffuse lower abdominal tenderness on palpation, the presence of a palpable, fixed, hard, presacral mass roughly 10 cm in diameter, and left cervical lymphadenopathy. Results of diagnostic studies showed a hemoglobin of 13.7 g and a white blood cell count of 11,000/mm<sup>3</sup> with normal differential leukocyte morphology. A chemistry survey, a chest roentgenogram, and a plain roentgenogram of the abdomen were interpreted as normal. An intravenous pyelogram and a CT scan of the pelvis revealed a large presacral soft tissue mass, displacing the urinary bladder anteriorly.

Subsequently, an exploratory laparotomy was performed. A biopsy of the pelvic tumor was diagnosed as showing "non-Hodgkin's lymphoma," which was strongly methyl green pyronine positive and stained negatively in the presence of anti-kappa and anti-lambda light chains and anti-lysozyme antibodies. The mass was unresectable, and diverting colostomy was performed. Thirty lymph nodes from the small bowel mesentery, periaortic areas, and iliac regions, and multiple liver biopsies were histologically non-neoplastic. A bone marrow biopsy and aspiration were also interpreted as normal.

Radiotherapy to the pelvis, and chemotherapy with cyclophosphamide, vincristine, and prednisone were initiated. Moderate abdominal pain persisted, and symptoms of urinary retention appeared in May 1978. In addition, the patient began to complain of numbness and dysesthesia in the left buttock and leg. A repeat CT scan in mid-June 1978 showed no diminution in size of the presacral mass, and left mediastinal lymphadenopathy was noted on a chest roentgenogram three weeks later. Adriamycin was added to the chemotherapy regimen.

Fever, nausea and vomiting, dyspnea, and severe abdominal pain prompted the final hospital admission in July, 1978. Temperature orally was 38.9°C — (102°F), the pulse was 144/min, and respirations were 44/min. The patient was cachectic and in moderate respiratory distress. Results of laboratory tests showed a hemoglobin of 11.7 g, white blood cell count of 10,800/mm<sup>3</sup>, and platelet count of 70,000/mm<sup>3</sup>. The chest roentgenogram revealed a large right pleural effusion and mediastinal lymphadenopathy. The serum sodium was 129 meq/l, and potassium was 6.7 meq/l. The serum creatinine was 3.1 mg%. The patient was treated symptomatically and he expired 3 days later.

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A complete autopsy showed massive lymphomatous infiltration of lymph nodes, spleen, liver, gallbladder, peritoneum, mesentery of the bowel, testes, pleura, and pericardium. In addition, microscopic involvement of the kidneys, sciatic nerves, periadrenal tissue, meninges, and lung parenchyma was identified. A huge tumor mass encased the bladder and rectum and filled the pelvis. The bone marrow was essentially completely replaced by lymphoma cells, and a smear of peripheral blood taken at postmortem examination disclosed lymphoblastic leukemia (Figures 1-3).

Histologically, the neoplastic cells were 10-15  $\mu$ m in diameter. The nuclear chromatin was finely dispersed, and the nuclear membrane showed a creased or convoluted appearance (Figure 4). Nucleoli were not prominent, the nuclear membranes were thin, and “starry sky” appearance of involved lymph node tissue was not observed. The cells contained only a scanty amount of cytoplasm.

### Discussion

The histopathologic features of the lymphoma cells in this patient are quite typical of those seen in LL. The rapid clinical progression of disease, age, sex, and the

refractoriness of the lymphoma to chemotherapy are all substantiating factors supporting this histologic diagnosis. In addition, the bone marrow and peripheral blood findings at postmortem examination were quite characteristic. The convoluted appearance of the nuclear membrane in neoplastic lymphoblasts is almost pathognomonic of this disorder.<sup>6</sup> However, not all cases of LL have this morphologic finding. Nathwani et al. reported it in only 50% of their cases.<sup>5</sup>

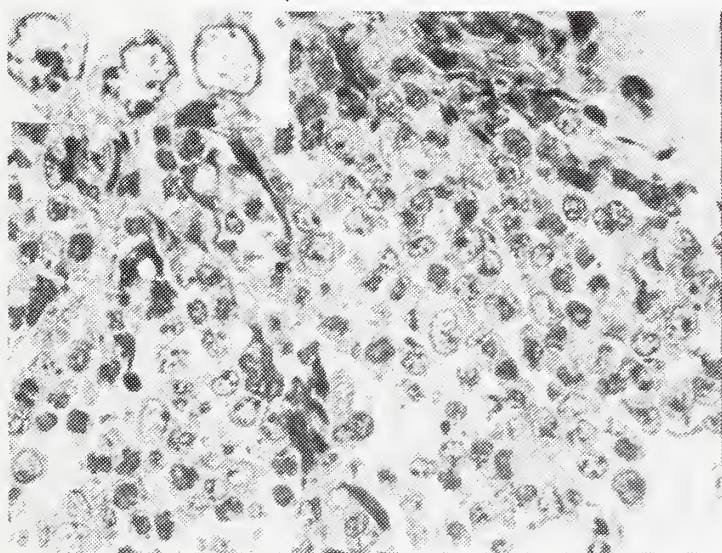


Fig. 1 — Photomicrograph of pelvic mass, showing large lymphoma cells with evenly dispersed chromatin and convoluted nuclear contours (inset). (Epon resin and Toluidine blue, X 400; inset X 900).

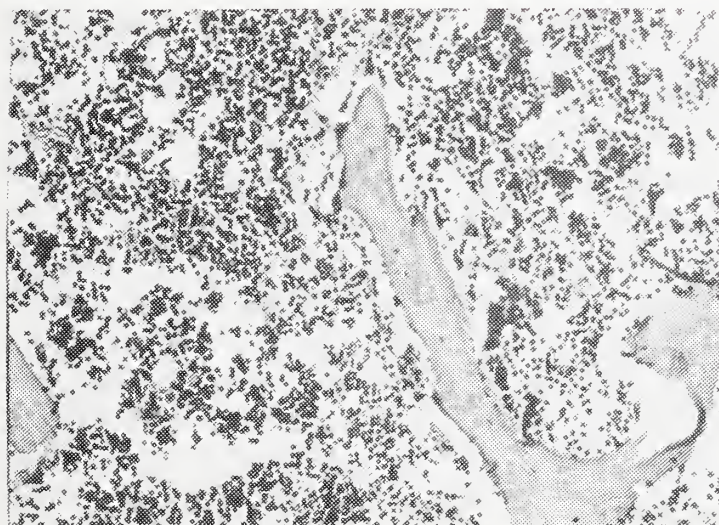


Fig. 2 — Massive replacement of bone marrow by large, densely-staining lymphoma cells, lymphoblastic type. (Hematoxylin and Eosin, X 60).

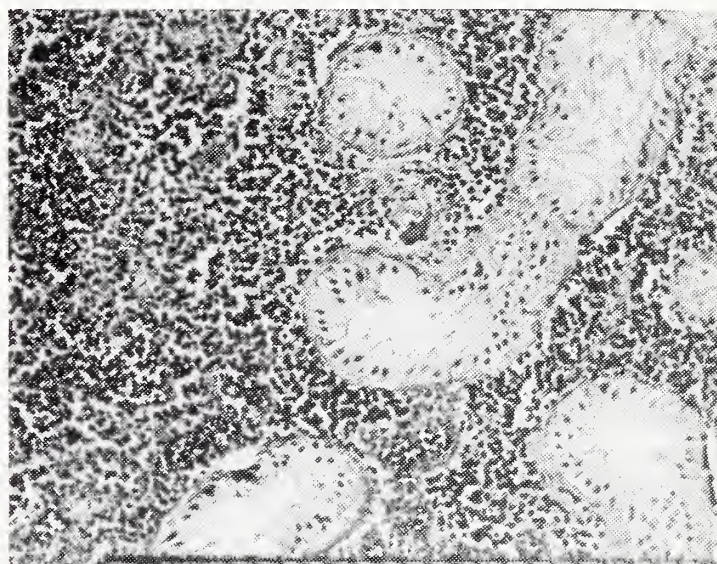


Fig. 3 — Infiltration of testicular parenchyma by lymphoma cells. These cells engulf but do not invade the seminiferous tubules. (Hematoxylin and Eosin, X 60).

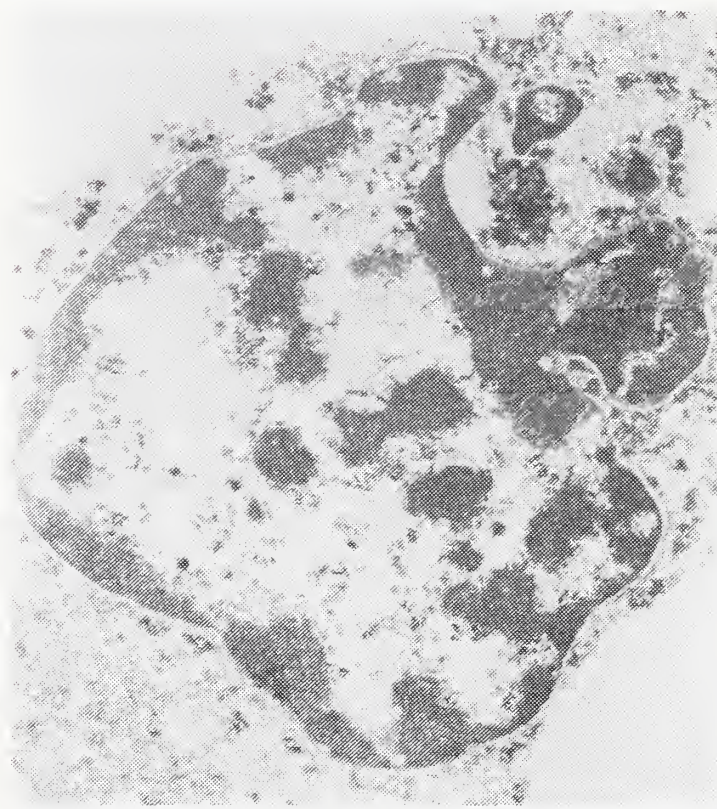


Fig. 4 — Electron photomicrograph of a lymphoblastic lymphoma cell. Note the paucity of cytoplasmic organelles, and the nuclear “blebs” that are typically seen in lymphoblastic lymphoma. (Uranyl acetate and lead citrate, X 10,000).



In the remaining group, the nuclear contour was smooth and ovoid.

It is in this latter group of cases of LL that special studies, including electron microscopy, are diagnostically helpful. Ultrastructurally, nuclear chromatin is dispersed without margination, and cytoplasmic polyribosomes are numerous.<sup>7</sup> Cells from lymph node suspension in 50% of cases of LL form rosettes with sheep red blood cells at 4° and 37°C.<sup>2,3,4,7</sup> Stains for cytoplasmic acid phosphatase are often positive. As in this case where there was focally positive staining in regions of the Golgi apparatus. In addition, the fluorescent antibody assay for terminal deoxynucleotidyl transferase is almost always positive, as test is quite specific for T cell disorders, particularly lymphoblastic lymphoma.<sup>8</sup>

Although extramediastinal masses are frequent (50%) in LL patients upon initial diagnosis, a pelvic tumor is quite rare. The most common lymphoma first appearing as an abdominopelvic mass in a youngster would be Burkitt’s lymphoma, a neoplasm of B cell origin.<sup>9</sup> However, the prominence of nucleoli in Burkitt tumor cells, the clumping of chromatin at the nuclear membrane, and the almost universal “starry

sky” microscopic appearance of affected lymphoid tissue in Burkitt’s lymphoma make confusion with LL unlikely. Additionally, one would not expect negative staining for light chain immunoglobulin in Burkitt’s lymphoma.

### Summary

Lymphoblastic lymphoma is a distinctive, aggressive neoplasm found in adolescent patients. Though it is commonly conceptualized as being associated with a mediastinal mass upon initial diagnosis, only 50% of cases may show this feature. Thus careful histopathologic examination and special studies are warranted in all cases of undifferentiated non-Hodgkin’s lymphoma affecting young people, regardless of the anatomic distribution of disease. In this manner, diagnostic error can be minimized, and appropriate therapy may be instituted early in the clinical course.

### Acknowledgments

The authors acknowledge their indebtedness to Drs. C.Y. Li and P.M. Banks for their critical review of the manuscript.

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### Second Annual Competition for Bush Clinical Fellowship Application due date: March 1, 1980

Up to fifteen *primary care* physicians from *non-Metropolitan* areas of Minnesota will be selected to receive grants. The purpose of these grants is to enable physicians to take 6- to 12-month, “sabbatical”-type leaves from their practices in order to improve clinical, administrative and leadership skills that would enhance health care delivery in their respective communities and also further their own professional goals. For more information and application forms, please write to The Bush Clinical Fellows Program, Box 715, 420 Delaware Street SE, Minneapolis, Minnesota 55455 (phone 612/373-8012).



# History

## “The General”

### A History of Hennepin County Medical Center

Part II\*

TIMOTHY J. RUMSEY, M.D.†

To most of us, the new facilities will always be “The General”. After all, it was so for over fifty years. To a select few, it still goes by “City Hospital”. When Dr. Joe M. Neal, an intern there in 1916 and acting superintendent in 1919, first saw the new medical center in July of 1976, he remarked “So that’s the new City Hospital.”<sup>28</sup> Dr. Neal also recalls the first name change. He states that when Dr. Walter List (formerly with the Cincinnati General Hospital<sup>29</sup>) took over as hospital superintendent, one of his first acts was to change the name to Minneapolis General Hospital. With the transfer of hospital operations to the County, in 1963, Hennepin County General Hospital was born. In 1975, anticipating the move to new facilities, the name was changed to Hennepin County Medical Center. This evolution of city hospital to county hospital is an extremely important chapter in the history of the General.

The following four hospital names reflect changes:

Minneapolis City Hospital	1887-1920
Minneapolis General Hospital	1920-1963
Hennepin County General Hospital	1963-1975
Hennepin County Medical Center	1975----

As previously noted, expansion planning began in the 1930s, but the following war years postponed any serious improvements. By the early '50s the hard facts were glaringly evident. The General had long since outgrown its dilapidated structures and the City of Minneapolis was shouldering a tremendous financial burden. While thought was given to a new hospital, with city and county support, it was seriously entertained that perhaps General Hospital was not needed at all and its various services could be performed by the University of Minnesota Hospitals and other private institutions. Thus, was launched an eloquent campaign by a diverse crowd of citizens and public interest groups to save the General. Government task forces examined the feasibility of keeping or abandoning the General.

As early as 1952, County Commissioner Richard O.

Hanson had proposed that the county take over the General.<sup>30</sup> One year later, the Citizen’s League of Greater Minneapolis recommended improvements to the existing facilities under city and county support.<sup>31</sup> The Hennepin County Medical Society shared backing for this plan. As some internal improvements took place, the need for county intervention increased. By 1963, it was felt that Minneapolis General Hospital would be phased out completely if not rescued by the county. Further indication for county rule was stated in the hospital services extended beyond the city proper and that the General could not be replaced as a training center in its care of the indigent or as an emergency referral center. Mr. George D. Dayton, Chairman of the General Hospital Task Force, and Mayor Arthur Naftalin urged the '63 State Legislature to facilitate



“The General”

\*See Part I, January, 1980 issue, page 17.  
†St. Paul, Minnesota.



this takeover. These recommendations were followed and the Hennepin County General Hospital became a reality. Unfortunately, it did so with even more outdated facilities.

Once decided that the General was in county hands, the drive for a new hospital could finally be launched. It culminated in a 10 : 1 voter approval for a 25 million dollar bond issue in 1969. Private citizens, as well as public interest groups, had waged a personal battle for this first referendum. The Hospital Service League led three tours daily of the building for nearly a year to make the facts available to the voters.<sup>32</sup> Eleanor (Mrs. Phillip) Pillsbury, 1st President of the Service League, personally pleaded with the community for a new hospital. Even in her last year, while dying of cancer, she raised money to underwrite the study which led to the first referendum.<sup>33</sup> Mrs. Pillsbury would never see the fruits of her labor when the new hospital opened some 89 years after the former Mayor George A. Pillsbury (her husband's grandfather) had supported a resolution to establish the first city hospital in 1887.

An interesting footnote to the General's troubles in the early '60s is the story of a former patient's attempt to lighten some of the hospital's financial problems. Mr. Ward Canfield, a Minneapolis policeman who was injured in a gun fight while on duty in 1957, had undergone surgery 15 times at the General. Being anxious to do something in return, he and five hospital physicians were party to a plan to operate a liquor store on Lake Street, with profits going directly to the General for medical research and other services. Canfield would manage the store and would be the only

salaried member of a non-profit organization designed to oversee the project. Despite the possibility of generating \$300,000 a year for the hospital, the plan met with legal and political entanglements and died a noble death shortly thereafter.

As if the General didn't have enough problems, inflation, rising construction costs, and a loss of



Minneapolis City Hospital, 1905.



Hennepin County General Hospital



The First "General"



anticipated federal funds rendered the 25 million dollar bond insufficient by 1971. A second referendum, for an additional 18 million dollars, was defeated and any thought of a new County Medical Center seemed doomed. Meanwhile, another study by the Citizen's League, completed in 1970, showed that the General and the expanding Metropolitan Medical Center could share certain facilities. This arrangement could further benefit MMC in its application for a certificate of need, necessary to be declared eligible for government funding.<sup>34</sup> After the defeat of the second referendum, the Metropolitan Health Board (an arm of the Metropolitan Council) issued these guidelines based on the Citizen's League's findings:

1. Hennepin County should build a new total patient care facility.
2. The new hospital should be located near and architecturally integrated with the Metropolitan Medical Center.<sup>35</sup>

In June of 1971, representatives from both hospitals met with architects in week-long intensive planning sessions to develop what would become the nation's first public-private medical complex. The hospitals would be separate entities involved in a shared venture, rather than an identity losing merger. Construction and operating costs were cut back by the bridging “Center Hospital” which physically joins the two institutions.

It is interesting to note from an historical view the recommendations of Mr. James A. Hamilton, hospital administration specialist at the University of Minnesota. In his 1952 Hamilton Report, he advised unifying Minneapolis hospital services to improve care and cut costs. He proposed a “Hennepin Hospital Center” as a grouping of hospitals around the then existing site of Swedish and St. Barnabas (now MMC) to co-operate in central purchasing, laboratory, laundry, and other joint services. He maintained that a General hospital in such a group should remain a public hospital.<sup>36</sup>

Metropolitan Medical Center and Hennepin County Medical Center have remained separate institutions with an innovative sharing venture. Hennepin's Chief of Medicine, Dr. Alvin Schultz, maintains that “the tie-in with a private complex has assured the future of an important health resource and the preservation of a major teaching hospital.”<sup>37</sup>

### **Always A New Beginning**

Actual construction of the new medical center began in the late summer of 1972. On May 5, 1976, it was ready for occupancy. One year of intensive planning had been completed for the big move. Forty ambulance

trips and forty-five van loads were used to transport the hospital residents, including 220 patients, to the new facilities located two blocks away and the whole process was over in hours.

This was actually the second move in the General's history. The first was on October 16, 1893, when patients were transported from the original hospital to the reconverted Brackett homestead. It is recorded in the Minneapolis Journal as follows: “The City Hospital was occupied today for the first time. Two ambulances were required to transport the patients from the old building to the new hospital on the Brackett property. By noon, 16 of the 53 now in the City Hospital had been transferred, together with many of the nurses. Many of the fever patients and others that are seriously ill will not be removed until their condition is improved and becomes such that removal is with no danger to the patient's health. It is probable that it will be the first of November before all of the patients are removed to the new building.”<sup>38</sup>

### **Vital Link with the University of Minnesota**

From its beginnings eighty-nine years ago, the “General” has always enjoyed a special relationship with the University of Minnesota Hospitals and Medical Schools. In 1871, Bishop Knickerbacker, whom we met as an early champion of health care for the poor, made the prophetic statement that “the time is not far distant when a medical faculty and a medical school must be connected with the rising University of Minnesota. A hospital is indispensable for such a school.”<sup>39</sup>

Indeed, the Hennepin County Medical Center and the University of Minnesota Medical School were to grow side by side, with the Medical School beginning in 1883-4 and the General in 1887. Informal teaching at General by University Medical faculty began as early as 1889 and was soon formalized, so that by 1908, the General Hospital's annual report could state “it was fortunate for the University Medical School that it could make the teaching arrangement with the City Hospital (General), and further, that it was also a distinct advantage to the hospital.”<sup>40</sup>

Chief of Surgery, Dr. Claude Hitchcock holds that the cornerstone from which the General derives its excellent reputation as a teaching hospital “is this commitment and dedication to teaching and the vigor and vitality of all these young people” and that will keep this hospital in the forefront and will maintain it with the spirit that has been so outstanding over the



years.”<sup>41</sup>

Twice, the Regents of the University had hoped to persuade Minneapolis to locate the General in close proximity to the school for the benefit of both parties. First in 1891, before the move to the Brackett site, and then in 1924, they offered to secure land adjacent to the campus where a new General could be erected. Both offers were eventually rejected, but the closeness of the two institutions has continued to the present.

Formal internships began with the opening of the first hospital in 1887, with only two positions available. The residency program began in 1921; its original participants not receiving any pay. After 1930, the University paid all resident salaries at the General.

All of the departments at General developed in close association with their counterparts at the University. Radiology, pathology, and anesthesiology depended upon the University for their lifeblood. Drs. S. M. White and E. T. Bell were instrumental in setting up the General's laboratory and Dr. R. T. Knight was equally influential in the anesthesia department. Many of the early specimens in the University's pathology museum came from the General. The School of Nursing at the General also enjoyed a symbiotic association with the University. Today, that vital link between all departments of the General and the University continues. Full-time General staff are part of the Medical School faculty and residents and interns are official Medical School graduate students. The intern staff had always predominately been made up of University of Minnesota graduates and it is a very rare medical student who does not have at least one clinical rotation at the General. Forty-five per cent of all specialists in Hennepin County received all, or part, of their advanced training here. Twenty per cent of all general practitioners and ten per cent of all the doctors in the state interned here.<sup>42</sup>

Many notable University staff have graced the General's halls as consultants. Among them have been: Dr. Robert Good, Dr. Wesley Spink, Dr. J. L. McKelvey, Dr. J. A. Myers, Dr. Robert Ulstrom and Dr. Cecil Watson. Dr. Owen Wangenstein was an extern at the General and the present dean, Dr. Neal Gault, was a former intern. Dr. George Fahr, the General's Chief of Medicine from 1927 — 1949, was, at the same time, a distinguished professor at the University. He had also participated in some of Einthoven's earliest work on the EKG while studying in Europe.

### Echoes from the Walls

1887 Minneapolis City Hospital opens

1889 “Because of inadequate fire protection, a fire brigade of employees has been organized.”

1893 The move to the Brackett property  
On the establishment of a nursing school: “A request for a skeleton, mannequin and a few elementary books on medical subjects . . . would not seem to be an extravagant request.”

1894 “Two tents were put up on the lawn to furnish accommodations for typhoid fever and other contagious cases. We feel this outdoor treatment of fever cases to be of great advantage.”

1895 “Sleeping rooms for nurses should be provided where they might obtain the necessary rest . . . away from the direct exhalations from the lungs of patients sick with diphtheria, scarlet fever, etc. . . .”

1897 A sampling of patient occupations:

Blacksmith	7	Tinsmith	3
Shoemaker	4	Magnetic Healer	2
Peddler	3	Showman	5
Baby	55	Millwright	1
Cooper	5	Harness Maker	3
None	31	Traveler	1
Tanner	1	Cigar Maker	1

1898 Construction of Out-patient Building

1901 Addition of East Wing

1902 On the hiring of student nurses: “They must be of sound health and without domestic encumbrances . . . must be prepared for an examination in reading, penmanship, simple arithmetic and English dictation to test their ability to read aloud well, to keep simple accounts, to write legibly . . . .”

“We feel especially grateful to the Police Department for their very efficient police ambulance service . . . of course, a covered wagon would be an improvement . . . .”

A sampling of diseases and surgical cases:

Actinomycosis	1	Cut throat	3
Balanitis	1	Gumma of the	
Bilious fever	1	Brain	1
Bubo	4	LaGrippe	1
Bunions	13	Plumbism	1

1902 “The present hospital ambulance is in bad condition and should be replaced, however, so long as we only handle sick cases and can travel slowly there is no danger and we can get along until the Board's financial condition will permit a change.”

1908 Because of strain on machinery, X-rays only taken on alternate days.  
Administration Building opens



- 1912 Hopewell Hospital established (T.B. Center in North Minneapolis, name changed to Parkview in 1920).
- 1913 Nurses Residence built (later named Harrington Hall).  
West Wing added
- 1914 Lymanhurst Children's Hospital occupied  
On overwhelming social services workload:  
“One person trying to help 750 patients must fall far short of what one would wish . . .”  
“The fee for social service home visits is 10 cents per patient visit, although free to those who cannot pay.”
- 1916 On social workers' duties: “To discover social causes that have forced the patient to the hospital . . . intemperance, overwork, under-pay, unemployment, passion for pleasure, ignorance of American standards of living, accidents, old age, lack of education, poor housekeeping, alone in the city, lack of parental discretion or responsibility, and ignorance of laws of hygiene . . .”
- 1917 Construction of a contagion building (later named the Annex)  
Addition of the laundry
- 1924 “The first female interns have arrived.”
- 1932 On the proposed 18-to-20 story modern hospital superstructure: “Modern hospital construction tends toward the perpendicular rather than the horizontal . . . patients are thus farther removed from the dust and noises of modern industry, and the air they breathe is said to contain . . . a much higher quotient of oxygen and less carbon monoxide and other injurious gases.”  
Tea served informally once a week in the second floor lounge  
“Patients are now permitted to smoke and play cards in the ward. Also allowed to have their own radios with both ear telephones and loudspeaker connections.”
- 1933 “Our buildings at the General Hospital are for the most part old . . . and costs and upkeep grow each year.”
- 1940 Sister Kenny begins work at the General
- 1945 Five floors are added to Harrington Hall
- 1947 Extra pay given for working on a TB ward
- 1949 The Annex is expanded
- 1958 Medical Research Laboratory constructed.
- 1963 Hospital operations are transferred from City to County.



Hennepin County Medical Center



- 1969 25 million dollar bond issue is approved.
- 1971 Hennepin County General Hospital and Metropolitan Medical Center begin sharing plans.
- 1976 New Hennepin County Medical Center opens.

### Where Are They Now?

The original City Hospital building was moved from its 11th Ave. location to 2001 9th Ave. S. in 1894. There it became a private home for several different families. It was torn down in 1973. The Brackett homestead, of course, was used as part of the actual hospital facilities from 1893 to 1906. At that time it

was razed for the construction of the main building. Hopewell Hospital in North Minneapolis functioned as a City operated and privately owned nursing home after 1930. It still stands at 512 49th Ave. S. and is operated by the Baptist Church.

### Summary

From a rented home to a reconverted farm site to a famous General Hospital to an innovative medical center. This has been the story of the General's first ninety years. Ninety years of solidifying a tradition and a pride to carry into the next century.

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# Minnesota Department of Health

## Formaldehyde in the Home Some Environmental Disease Perspectives

VINCENT F. GARRY, M.D.\*; LAURA OATMAN, M.S.†; RICHARD PLEUS††; and DAVID GRAY, M.P.H.‡

**Formaldehyde is an ubiquitous chemical with a potential for environmental disease in the home.**

IN THESE TIMES of "fouling our nest" with chemicals, we must judge the benefit of their use against their risk to our health; we must decide whether or not control measures are economically feasible. Many of the chemicals are new, the products of recent research and development; some are older. In the latter category is a chemical called formaldehyde. While it has been well known and long used as a biologic fixative, formaldehyde has recently come to the fore because of its use as a component of home insulating material and in the fabrication of particle board; a product used as a wood substitute. These items are not an inconsequential benefit in our current energy crisis. However, like all chemicals, formaldehyde has its risks and adverse effects. Some of these are known; others are potential and require further investigation. It is the purpose of this paper to inquire into these known and potential risks.

Formaldehyde is an ubiquitous chemical that has been present in the earth's environment since its earliest beginnings. Formation and degradation of this chemical is part of the routine metabolic processes of most species, including man. The study of formaldehyde effects began as early as 1640 when Fischer, a noted chemist of his day, began to investigate a component of insect venom, formic acid.

Aside from this very early investigation, formaldehyde effects have been documented through its use.<sup>1</sup> Industry, even before the turn of the century, has used this chemical for a wide range of processes. Leather tanning, embalming, tissue preservation and the manufacture of textiles are among the most innovative

and successful uses of this chemical. In the present era, formaldehyde has found its way into the home as a component of particle board, adhesives, shampoos and urea-formaldehyde foam insulation.

Because of the current socioeconomic stresses, particle board is widely used in the mobile home industry. Floors, walls and cabinetry are made of this material. To ensure energy efficiency, these homes are tightly sealed in accord with government regulation. In the same sense, standard homes have been made more energy efficient through incorporation of formaldehyde-foam insulation because of its high heat retention value and relatively low cost.

Despite the numerous advantages of these new materials, there are some noteworthy drawbacks. Particle board is formed by the unique bonding of wood shavings with polymerized complexes of urea-formaldehyde. However, the polymer is somewhat unstable. Free formaldehyde gas is trapped in the material and given off in ever-increasing quantity by elevation temperature and humidity.<sup>2</sup> Not only ambient conditions within the home, but also seasonal temperature/humidity fluctuations in the atmosphere will affect the rate of offgasing. On site installation of formaldehyde-foam is also affected by ambient environmental conditions. Polymerization of the foam may vary with alterations of temperature and humidity unless these factors are properly addressed during the mixing operation. Furthermore, the material will break down with the release of formaldehyde gas in the presence of water.<sup>3</sup> Yet, particle board and foam insulation are not the only sources of formaldehyde gas in the home. Carpeting and drapes may also be a significant source of this irritant gas.

For several generations the irritant effects of formaldehyde have been well documented in industrial/occupational settings by a number of medical investigators. Most commonly, eye, nose and throat irritation are observed. Concentrations as low as

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0.2 ppm may produce these symptoms in the newly exposed individual.<sup>4</sup> With continued exposure the irritant effects may subside, indicating accommodation to low concentrations of the chemical. However, with re-exposure, symptoms recur. Significant effects on pulmonary function in non allergic individuals are infrequently reported. Most have been accidental or intentional exposure<sup>5</sup> to high concentrations of the gas, exceeding maximum human tolerance level of 20 ppm. At this concentration, studies indicate that individuals will remove themselves from the source of exposure within five minutes. Interestingly, perception of formaldehyde odor occurs at 0.05 ppm,<sup>6</sup> a concentration below the detection limits of routine analytic instrumentation.

On the basis of the irritant effects of formaldehyde, the Occupational Safety and Health Administration (OSHA) has set a time weighted exposure limit of 3 ppm. However, the National Institutes for Occupational Safety and Health (NIOSH) has recommended a reduction of that limit to 1.0 ppm. These levels do not consider persons with skin or respiratory allergies to the chemical. A recent publication in the American Industrial Hygiene Journal recommends a further reduction of the limit to 0.1 ppm, a concentration at which no irritant effects are observed.<sup>7</sup>

The foregoing brief account of the human effects of formaldehyde and its regulation in an industrial setting may not be applicable to exposure in the home. In this situation, persons exposed include young children, infants, pregnant women, persons with chronic disease, including asthmatics and other allergic individuals. Exposure is not limited to an eight hour day, but occurs continuously at a low dose for months or years. Because most mobile homes are tightly sealed and do not use a continuous influx of outside air for heating, other air pollutants such as CO and NO<sub>2</sub> may accumulate and so contribute to the environmental disease potential of the home environment.<sup>8</sup>

With this background in mind, investigative efforts have been initiated at the federal, state and local levels to define the health effects of formaldehyde in the home environment. In this present report, we will describe our initial findings based on interviews of the exposed population who voiced complaints and measurement of the ambient formaldehyde levels in the homes.

## Materials and Methods

### Study Population

Between February and June, 1979, 275 cases of

possible formaldehyde exposure were reported to the Minnesota Department of Health. All of the cases were screened by an initial physician interview and followed up by a visit to the home site where indicated. At that time, persons were again interviewed by another staff member and the ambient level of formaldehyde was measured. Where possible, clinical summaries of the patient's condition were obtained from the local physician. For the purposes of the study, the population was apportioned by age and sex: Newborn through two years (24 males, 12 females) children, ages three through 13 years (21 males and nine females); adolescents through adults (48 males and 54 females).

## SYMPTOMS REPORTED

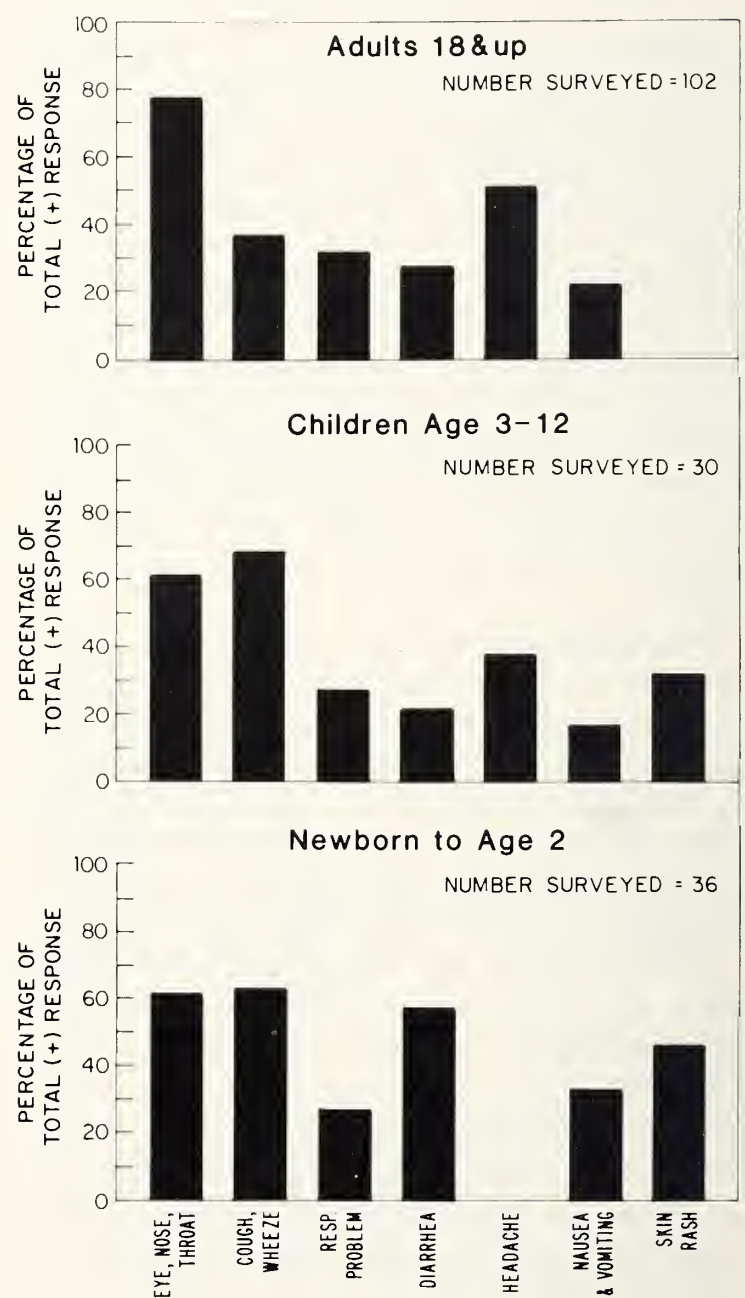


Fig. 1 — The frequency of symptomatology in the study population is recorded on the graphs above according to the age groups listed.



### Interview Methodology

To establish possible exposure to formaldehyde and relationships to direct and indirect effects, all families with a member who related index symptoms (i.e. eye, nose and throat irritation) were asked to supply detailed medical historical data. This included an organ system review, past history and pregnancy information. Environmental data, including the age of the home, type of home, type of insulation and heat used in the home, was also obtained.

### Formaldehyde Analysis

Air samples were taken with a mini-impinger for a half hour period at a distance of approximately 50 cm. from the floor. Measurements were obtained from the living room and the bedroom of each home. Analysis was conducted according to the standard NIOSH method for formaldehyde. Measurements were made on site on a one time basis.

### Results and Discussion

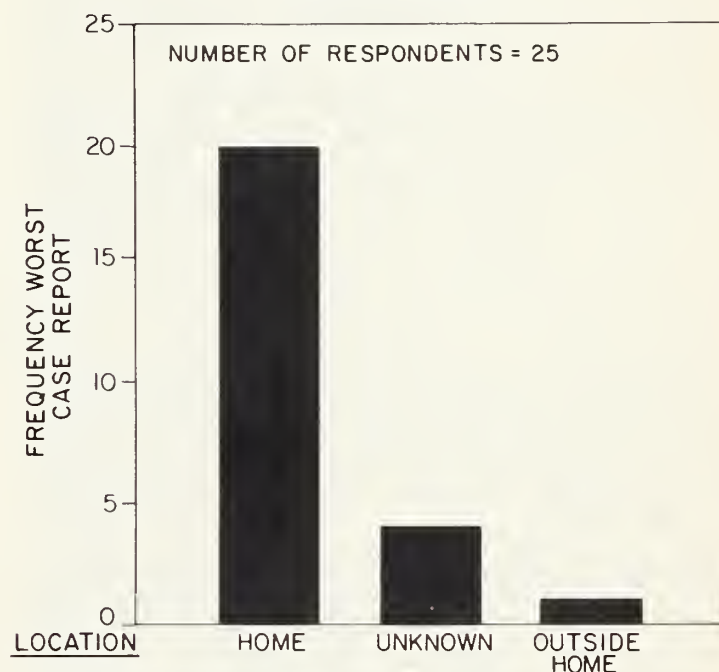
The symptomatic reports illustrated in Figure 1 describe the variation in symptomatology on the basis of age. Other non-environmental factors may have contributed to the symptoms reported. However, alteration of symptomatology by change of location and season indicate a primary environmental effect in the home setting Figure 2 (a) and (b). Furthermore, the mean formaldehyde concentration in the homes of those persons who reported index symptoms (i.e. eye, nose and throat irritation) is significantly higher than non-symptomatic individuals' homes. It is of interest to note that persons with a history of asthma tend to report effects of exposure at a lower dose.

This is consistent with the concept that formaldehyde may be a triggering event for asthma<sup>9</sup> or may in some cases be an allergen via hapten-protein combination.<sup>10</sup> On the other hand, persons who are smokers are relatively insensitive to the irritant effects of formaldehyde. Tobacco smoke, in addition to its content of aromatic hydrocarbons, also contains a number of respiratory irritants, including formaldehyde.<sup>11</sup> Perhaps, as indicated by occupational studies, accommodation to continuous exposure to formaldehyde occurs among this segment of the population.

As indicated in Figure 1, upper respiratory symptoms are increasingly reported by younger age groups. In general, respiratory irritants have an effect on respiratory rate and susceptibility to respiratory infection. Reflex slowing of respiration has been used to generate dose response effects of formaldehyde in rodents, and occurs within minutes of exposure.

Interestingly, other newborn mammalian species respond to environmental alterations by slowing respiration<sup>13</sup> (diving reflex). Animal studies have clearly shown that impairment of the immune response to infection occurs in the presence of irritant gases such as NO<sub>2</sub> and ozone.<sup>12</sup> Similar studies have not yet been reported for formaldehyde, but are forthcoming. In newborns and young children other factors, such as differences in the anatomy of the respiratory tract, respiratory rate, and stage of development, may influence the extent of respiratory symptoms by

WORST CASE DISCRIMINATION (SYMPTOMS) BY LOCATION



WORST CASE DISCRIMINATION (SYMPTOMS) BY SEASON

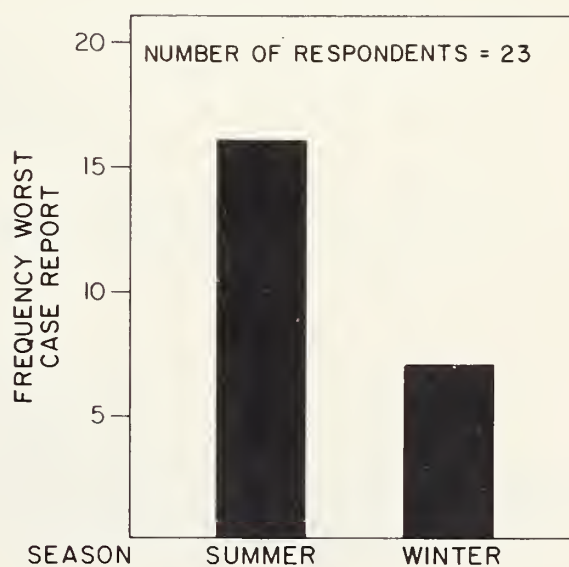


Fig. 2 — Worst case association by (A-top) change of location (B-bottom) season of the year.



alteration of the dose per unit time. Under these circumstances, young children could have a higher body burden of the chemical as compared to adults under the same conditions of exposure.

Symptomatic responses of diarrhea and headache present a diagnostic problem in most medical settings, including the environmental and occupational area.

Other studies <sup>14,15,16</sup> as well as our own have reported these symptoms and their possible relation to formaldehyde exposure in the home environment. However, other home air pollutants may make a contribution to the effects described. For example, it is well known that headache is the predominant finding after exposure to sublethal levels of carbon monoxide; a contaminant that may present in a tightly sealed home.

Variation in the levels of formaldehyde by age of the mobile home and season of the year are to be expected, Figures 3 (a) and (b)). Experimentally, the rate of release of formaldehyde from particle board is affected by ambient conditions of temperature and humidity. Over and above these factors, the type of particle board bonding agent (i.e. phenol/formaldehyde or urea/formaldehyde) affects the quantity of formaldehyde released. Fig. 3a shows that the mean formaldehyde levels per month from February through June varied with seasonal change, indicating temperature/humidity effects.

Figure 3(b) indicates that newer mobile homes tend to show higher levels of formaldehyde. This effect may reflect overall usage of formaldehyde releasing materials and/or a change in the bonding agent used.

More subtle effects of formaldehyde affecting

pregnancy have been studied by several Russian workers. Their study suggests no effect on prematurity or miscarriage rate among women textile workers exposed to formaldehyde.<sup>17</sup> In our preliminary survey, we found an 11.6% miscarriage rate among 86 pregnancies of 77 women reporting formaldehyde symptoms;<sup>18</sup> no different from that reported in previous studies of unexposed populations. The incidence of prematurity found in our survey was 11.7%. This incidence rate is somewhat elevated when compared to other studies of caucasian populations, but below that for blacks.<sup>19</sup> Since no attempt was made in this initial survey to determine racial origin of the study population or adjust for socioeconomic factors,

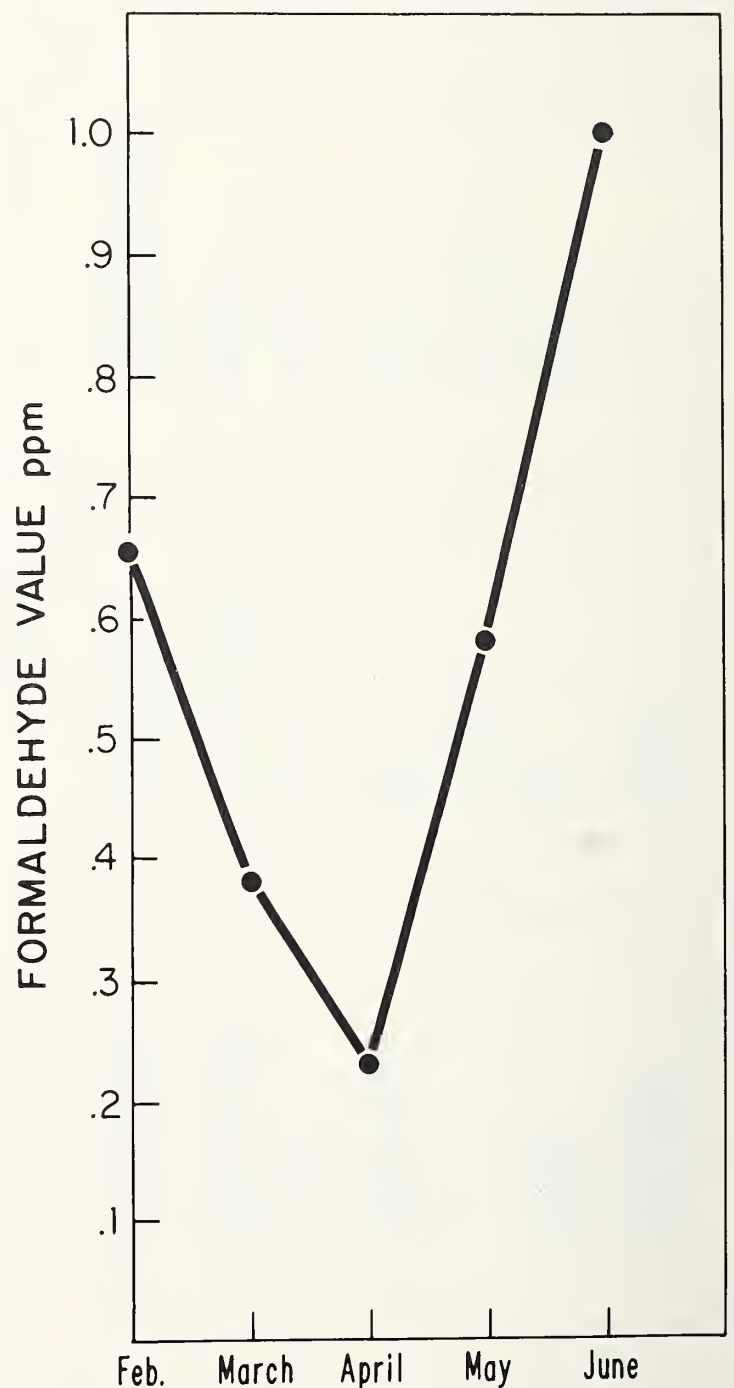
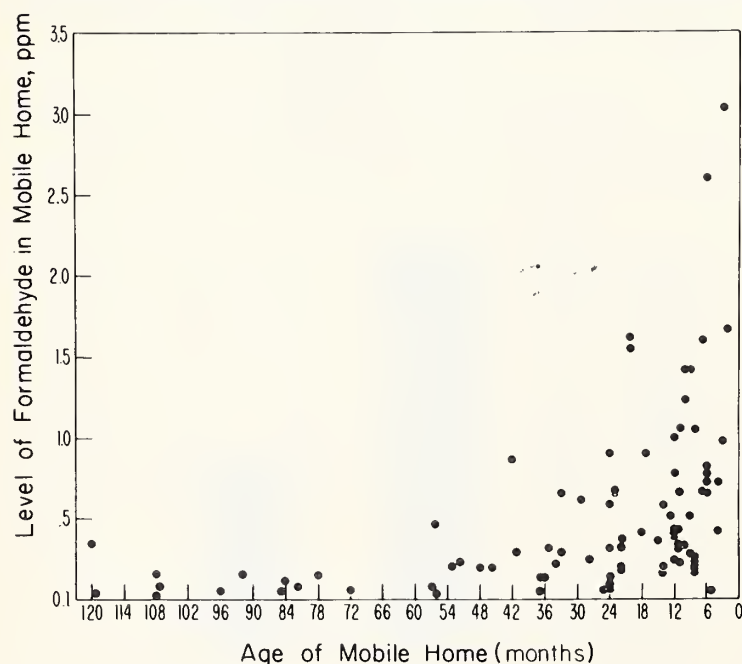


Fig. 3 — Levels of formaldehyde in mobile homes by (A-left) age of home and (B-right) mean values per month from February through June of 1979.



the apparent discrepancy may not be biologically significant. More definitive studies are needed in this area before this potential problem can be totally resolved. In the same vein, it is unclear whether any relationship exists between formaldehyde exposure and the occurrence of the Sudden Infant Death Syndrome (SIDS). Present data does not confirm or deny some subtle influence.

Although more complete descriptive studies and investigations of the long term pathophysiologic effects are needed to provide better understanding of the present problem, its solution may not involve a medical approach. As with other environmental and occupational hazards, prevention and control measures center on a reduction of exposure to a noxious chemical. Use of improved ventilatory procedures, sealants to prevent formaldehyde offgassing, absorbents to remove the chemical from the ambient environment or substitution of other chemicals for formaldehyde could substantially reduce levels of

exposure. Uniformly safe levels of exposure will only be determined through detailed long-term human and animal studies underway at several public and private institutions.

In any case, the findings reported here point out that energy consciousness should be matched by an awareness of the increased potential for the development of environmental disease. Careful, impartial evaluation of these present and future concerns will undoubtedly continue as we balance energy use and efficiency against the potential for environmental disease.

#### Acknowledgments

The authors wish to thank the physicians of Minnesota and their patients for supplying pertinent clinical data for these case studies. Special thanks to Dr. Hugh Westgate and Dr. Ralph Franciosi of Children's Health Center, Minneapolis for their cooperation and guidance. Finally, we thank the members of the communications media for their spirit of inquiry in bringing this problem to our attention.

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#### Cover Photograph

“Bassett Creek in February

Dr. Edward L. Kaplan's son, Mark, took the cover photograph. Mark is a 15-year-old going to school at Robbinsdale High School. His father is a Professor of Pediatrics at the University of Minnesota.

Bassett Creek is a stream which originates in Medicine Lake and flows through the northwestern suburbs of Minneapolis (including Golden Valley, where this photograph was taken); it eventually empties into the Mississippi River. During much of its course, the Creek is a haven for wildlife, including not only various species of fish, but wild fowl too. Other wild animals are often seen along its banks. In the spring when the water is high, the Creek is frequented by young people tubing down it, and in the winter when parts of it freeze over, one may observe skaters there.

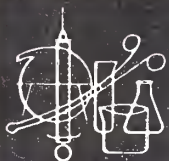
The picture was taken with a Kowa SE 35 mm single lens reflex camera, using Kodachrome film.



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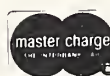


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# Minnesota Medical Association

## The Challenge of Change

Medical Ethics — Yesterday, Today, Tomorrow

GEORGE B. MARTIN, M.D.\* and WILLIAM JACOTT, M.D.†

Medicine's world seems to most of us as though it is suffering from crisis, shock. Changing technology, societies changing expectations, governmental legislation, rule and regulation spearheaded by the FTC's recent activities are a sum of stresses sufficient to cause even the most bucolic to react with anger on occasion. Given this climate, it is understandable that considering a change in the bedrock of our profession, the Code of Medical Ethics will cause strong reactions.

It is easy to forget that our code of medical ethics is entitled "The Principles of Medical Ethics". It was changed last in 1957 and five times since 1908. Change is upon us. Today suddenly has become yesterday and tomorrow is here.

What should medicine's ethics be? A code of behavior common to physicians in governing their responsibilities to peers, patients and society is the generally accepted concept. Not above the law, but consistent with it. Not a personal moral code, but based on common moral behavior with latitude for individual differences. Not a set of rigid rules or regulations, but a guide or principles applicable to the behavior of our profession. The current AMA proposal for the development of medical ethics by an Ad Hoc Committee of devoted and knowledgeable physicians states:

Preamble: This language establishes broad areas of responsibilities for all physicians and reaffirms the belief that ethical standards are for the benefit of the patient. To allow for maximal individual discretion and accountability, these statements are clearly guidelines open to interpretation and universal application.

- I. A concise statement of mission emphasizing the magnitude of a physician's commitment, and how it shall be met.
- II. This wording is a clear mandate for self-discipline, calling on the precepts of fairness and honesty toward all. The deceitful are to be exposed, the impaired helped, and the unscientific educated.
- III. Society should expect obedience to laws properly enacted, but the dedication of a physician requires lawful disagreement and attempts at modification of those laws inimical to sound patient care or contrary to accepted moral behavior.
- IV. Due process is constitutionally guaranteed. No one has, or should have, the ability to abridge the legally given rights of another. Similarly the professional relationship is predicated on trust, and the confidentiality of this relationship, within the constraints of the law, must be assured.
- V. Effective implementation of a physician's mission depends upon the application of sound scientific concepts, the ability of the public to make intelligent health choices, both as to procedure and person, and the liberal use of consultation with other health professions as may be indicated.
- VI. Within the framework of these Principles, the physician is entitled to certain rights which should not be denied if individual talents are to be developed to the fullest. Freedom of choice by physician and patient is essential.
- VII. Citizens should participate in community and societal affairs. By virtue of

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\*Chairman, MMA Speaker's Special Reference Committee on Medical Ethics.

†Co-chairman of the above committee.



special training, a physician, as a citizen, may have additional values and should recognize that possibility. Whether to exercise that citizen's responsibility always has been and should remain an individual decision.

In a future issue, the actual principles of ethics will be discussed. Your Minnesota Medical Association will hold a reference committee hearing at its Annual Meeting, May 1980, at which time your views on medical ethics will be heard as the first step in developing Minnesota Medical Association's position on the proposed AMA Principles of Medical Ethics. It is hoped that Minnesota's American Medical Association members will share their views with the reference committee. Your AMA delegation needs that support to be effective representatives for your tomorrows, not yesterdays.

## Nominees for State Offices

In cooperation with the House of Delegates, we are publishing the preliminary list of nominees for Minnesota Medical Association offices. In addition, any delegate may make nominations from the House of Delegates floor after the report of the Nominating Committee.

Each elected official will assume his position at the conclusion of the 1980 Annual Meeting. The current president-elect, John Meinert, M.D., was elected in 1979 and will become president after the 1980 Annual Meeting concludes.

The next issue of MINNESOTA MEDICINE will contain biographical material on all of the candidates.

### **President elect:**

Thomas G. Briggs, M.D. — St. Paul  
Charles J. McCarthy, M.D. — St. Paul.

### **First Vice-President:**

Dean Nywall, M.D. — Slayton  
Robert M. Wagner, M.D. — Minneapolis

### **Second Vice-President:**

Local arrangements chairman

### **Secretary:**

Richard P. Carroll, M.D. — St. Paul  
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# Special Article

## Neuropathies of Diabetes

### Part I. Symmetric Neuropathies

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Symmetric forms of diabetic neuropathy include peripheral sensory neuropathy and autonomic neuropathies. These may arise from metabolic abnormalities affecting nerves or myelin sheaths or both. Asymmetric neuropathies include cranial neuropathy, peripheral mononeuropathy, mononeuritis multiplex, plexus neuropathy, and radiculopathy. The asymmetric forms may arise from local insults such as vascular occlusion or trauma, affecting nerves made susceptible by metabolic derangements. The symmetric diabetic neuropathies with the subgroups sensory and autonomic are discussed in Part I. Part II is concerned with the asymmetric neuropathies: cranial and peripheral.

**D**IABETIC NEUROPATHY may afflict as many as 45% of diabetic patients.<sup>1</sup> Published series have reported that 13 to 30% of diabetic patients have both signs and symptoms of neuropathy,<sup>2,3</sup> while an additional 16% have signs without symptoms.<sup>2</sup> Although diabetic neuropathy is frequent and produces morbidity, the diabetic complication primarily responsible for tripling the mortality rate in the diabetic population is vascular disease.<sup>4</sup> Therefore, the goal in treating the neuropathy of diabetes is usually not so much to prolong life as to improve its quality.

The pathogenesis of diabetic neuropathies is still poorly understood. Classification of these clinical syndromes into symmetric and asymmetric forms presumably reflects differences in pathogenesis.

The symmetric neuropathies — primarily sensory polyneuropathy and autonomic neuropathy — may result from metabolic derangements.<sup>5</sup> One such derangement which has received recent attention is the possibility that accumulation of sorbitol in myelin contributes to the pathologic process of segmental demyelination by producing osmotic damage in Schwann cells.<sup>6</sup> Other studies have suggested that elevation of blood glucose levels may acutely impair nerve function by depleting the nerve's supply of myo-inositol,<sup>7</sup> a phospholipid-bound polyol that may modulate the interaction between calcium and sodium-potassium fluxes.<sup>8</sup>

Some of these same metabolic and pathologic

processes may make peripheral nerves and nerve roots more susceptible to other insults, such as pressure-induced trauma. Thus, one subset of the asymmetric diabetic neuropathies consists of mononeuropathies and radiculopathies due to passage of vulnerable nerves over trauma-exposed prominences and through pressure-prone spaces. The increased incidence of carpal tunnel syndrome, peroneal palsy, and Bell's palsy in diabetic persons is consistent with this concept.<sup>9</sup>

Another group of asymmetric diabetic neuropathies seems to arise from involvement of the vasa nervosa by microangiopathy. Some pathologic data suggest that this is a cause of diabetic mononeuropathies of the ocular motor nerves<sup>10</sup> and of mononeuropathy multiplex.<sup>11</sup> Plexopathies and radiculopathies of diabetes also may be caused in this manner.<sup>12</sup>

#### Sensory Polyneuropathy

##### *Incidence*

Thirty percent of diabetic patients have symptoms and signs of symmetric polyneuropathy, with predominance of sensory changes in the distal portion of the lower extremity.<sup>2,3</sup> This pattern accounts for more than 70% of neuropathy in diabetic patients.<sup>2,3</sup> The mean time interval between the onset of diabetes and the appearance of this form of neuropathy is five years.<sup>1,13</sup> However, 30% of diabetic patients with this neuropathy have evidence of it when their diabetes is diagnosed.<sup>2</sup>

##### *Symptoms and Signs*

Most patients are asymptomatic or have mild numbness and paresthesias in a stocking-glove dis-

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tribution. Symptoms are usually most prominent in the lower extremities. Dysesthesias occur with approximately half the frequency of painless paresthesias<sup>2</sup> and include burning (especially in plantar aspects of the feet), calf aching and cramping (relieved or unchanged by walking — unlike claudication), and lancinating pain. These dysesthesias are frequently worse at night and may be triggered or exacerbated by ordinarily innocuous stimuli (a phenomenon termed “hyperpathia”). When the neuropathy is severe, all sensory modalities have marked deficits. Sensory ataxia due to decreased proprioception occurs in this setting, as does motor weakness in the distal parts of the lower extremity.<sup>2</sup> Another nonsensory component in some patients is endogenous depression, producing anorexia and insomnia (a symptom complex usually occurring in middle-aged men who have mild diabetes and impotence).<sup>14</sup>

The most common signs of symmetric, primarily sensory polyneuropathy include loss of the Achilles tendon reflex (88%), diminished vibration and pin-prick sensation in the distal lower extremity (each 80%), and impaired light-touch sense (70%).<sup>2</sup> Position sense is decreased less frequently (43%); but when loss is extensive, Romberg’s sign is positive. The patellar tendon reflex is diminished in 28% of patients. Motor weakness of the feet is detectable in 12%, and sensory deficit in the hands is found in 5% of patients with this polyneuropathy.<sup>2</sup>

#### *Precipitating Factors*

The acute onset of diabetic sensory polyneuropathy may be precipitated by poor diabetic control,<sup>2</sup> by the establishment of adequate treatment of previously uncontrolled diabetes (either with insulin or diet),<sup>15</sup> and by various stresses (such as cerebrovascular accident) unassociated with worsening of diabetic control.<sup>16</sup> In all of these situations, the prognosis for improvement of the neuropathy over several months is good. Diabetic neurogenic cachexia (sensory polyneuropathy with impotence and depression-induced cachexia) generally remits within 1 year.<sup>14</sup> Recovery from insidiously progressive sensory polyneuropathy occurs in 30% of patients in whom diabetes becomes well controlled; no patient improves if the control of the diabetes remains poor.<sup>2</sup>

#### *Complications*

Sensory polyneuropathy may so thoroughly inhibit proprioception and pain sensation that joints of the lower extremity repeatedly suffer unperceived minor trauma. Persistence of this process destroys articular surfaces within an average of 18 years after the onset of

diabetes in as many as 6% of patients with diabetic neuropathy.<sup>17,18</sup> The arthropathy so produced is termed “neuropathic arthropathy” or “Charcot’s joints.”

Characteristically, diabetic neuroarthropathy affects the distal joints of the lower extremity.<sup>19</sup> This distribution differs from the pattern of tabetic neuroarthropathy (the most common cause of Charcot’s joints) inasmuch as tabes most commonly affects the larger proximal joints of the lower extremity.<sup>20</sup> Syringomyelia tends to involve the cervical vertebrae and the large joints of the upper extremity.

Symptoms and signs vary with different sites of involvement.<sup>19</sup> Patients with arthropathy of tarsal and tarsometatarsal joints present with bony deformities. Plantar deformity contributes to the formation of overlying callus. The callused areas are subject to ulceration and infection. Both plantar and dorsal deformities shorten and widen the foot (“cube-foot deformity”), prompting the patient to change shoe size. Approximately 17% of patients with tarsal and tarsometatarsal involvement have local redness, swelling, and warmth without pain. Limp is detectable in 30% of these patients.

Patients with metatarsophalangeal arthropathy usually present with ulceration of callused areas (60% of patients). Nearly 25% of these patients have hyperextensible joints, often with crepitus. Involvement of ankle joints produces soft-tissue swelling and, in 60% of patients, also causes limp.

Roentgenographic signs of Charcot’s joints include articular disruption (often with subluxation and metaphyseal and epiphyseal fracture and fragmentation), bony sclerosis adjacent to involved joints, pencilling of metatarsal and phalangeal shafts, and periosteal new bone formation.<sup>17,19</sup>

Like the plantar deformities of diabetic neuroarthropathy, other features of diabetic polyneuropathy predispose to the formation of pedal callus, with subsequent ulceration. Neuropathy affecting distal motor nerves produces weakness and atrophy of the intrinsic muscles of the foot. The most common result is “claw-toe” deformity (dorsiflexion of the toes at the metatarsophalangeal joints), which transfers the body weight onto the metatarsal heads. Callus develops, with subsequent ulceration over the metatarsophalangeal joints.<sup>21</sup> This process produces neurotrophic ulcers in approximately 30% of diabetic patients with symmetric, primarily sensory polyneuropathy.<sup>2</sup>

Characteristically, neuropathic ulcers are painless. They present with incidental discovery of an ulcer or of



its serous discharge. Examination reveals a punched-out ulcer with surrounding callus on a warm foot with palpable pulses. When pain accompanies diabetic foot ulcer, an ischemic contribution to the process should be suspected.<sup>22</sup> If the extremity is painful and if physical signs are consistent with compromised blood flow — diminished pulses, cold temperature, diminished vascular reflexes (rubor on dependency with blanching on elevation)<sup>23</sup> — then evaluation with the Doppler flowmeter may help in delineating the vascular contribution. Arteriography may be useful in planning therapy if Doppler studies are suggestive of compromised blood flow. Cultures and roentgenograms of affected areas should be obtained in order to evaluate the possibility of osteomyelitis.

### *Therapy*

Therapy in uncomplicated diabetic sensory polyneuropathy comprises: (1) attempts to minimize aggravating factors, (2) measures to prevent complications, and (3) symptomatic treatment. Poor control of diabetes is a major exacerbator of polyneuropathy. Achievement of good control is necessary, although not sufficient, for inducing at least partial remission of this type of neuropathy.<sup>2,13</sup> Another contributor to the severity of diabetic polyneuropathy is superimposition of drug-induced neuropathy by drugs such as nitrofurantoin, hydralazine, isoniazid, disulfiram, and diphenylhydantoin. If suitable alternatives are available, the use of these medications should be stopped (except for isoniazid, which should be supplemented with pyridoxine). A third factor that may aggravate diabetic sensory polyneuropathy is concurrence of a second neuropathy-associated condition, such as renal insufficiency, malabsorption, alcoholism, or myxedema. These should be considered in the clinical evaluation of the patient with symptomatic polyneuropathy.

Foot care helps prevent or retard trophic changes of diabetic neuropathy. The diabetic patient should inspect his feet daily for blisters, scratches, and cuts. These lesions should be washed with warm water and dressed with antiseptic and a sterile dressing. The feet should be washed daily in water the temperature of which is adjusted using a temperature-sensitive part of the upper extremity. Bland lubricating cream and talcum powder (the latter for the webs of the toes) should be used daily. The feet should remain warm, dry, and covered. The use of garters and excessively restrictive stockings should be avoided. Corns and calluses should be gingerly filed with an emery board, and corners of toenails should not be truncated. Shoes should not produce local irritation.<sup>24</sup>

When uncomplicated sensory polyneuropathy produces severe pain unresponsive to salicylate therapy, symptomatic treatment with fluphenazine, 1 mg three times daily, should be tried. If the symptom persists after 48 hours of treatment, amitriptyline, 75 mg at bedtime, may be added.<sup>25</sup> Both drugs can cause hypotension, and amitriptyline may precipitate urinary retention. Because of frequently coexisting autonomic neuropathy, patients with diabetic sensory polyneuropathy may be particularly sensitive to these side effects.

The treatment of trophic changes is generally conservative. In treating Charcot's joints, limitation of motion and weight-bearing by the affected joint is accomplished by application of a walking cast.<sup>21</sup> If the articular surface is subluxed but not totally destroyed, the immobilization may allow regrowth and realignment of the structures. If the joint surface is destroyed, the joint will heal by bony fusion.<sup>17</sup> Patients who have plantar bony protrusions will experience regression of overlying callus and ulcer with avoidance of weight-bearing. However, the deformity persists with conservative treatment. Callus and ulcer formation may recur with resumption of weight-bearing.<sup>19</sup>

Treatment of trophic ulcers includes limitation of weight-bearing, debridement, treatment with appropriate antibiotics, and trimming of surrounding callus. For recurrent disease, surgical resection of the involved metatarsal head is often helpful.<sup>21</sup>

### **Autonomic Neuropathy**

The symmetry seen in diabetic sensory polyneuropathy is also a feature of the autonomic neuropathy of diabetes. Although this symmetry probably reflects a metabolic etiology in both forms of symmetric neuropathy, axonal (rather than Schwann cell) derangements are more prominent in autonomic neuropathy.<sup>26,27</sup> Clinically apparent disease of the autonomic nervous system occurs in approximately 28% of patients with diabetic neuropathy.<sup>13</sup>

#### *Diabetic Anhidrosis*

The most obviously symmetric type of autonomic neuropathy is diabetic anhidrosis secondary to dysfunction of postganglionic sudomotor nerve fibers — a condition that affects approximately 10% of patients who have diabetic neuropathy.<sup>13,28</sup> The stocking-glove distribution of anhidrosis resembles that of sensory polyneuropathy, with predominant involvement of the lower extremities.<sup>28</sup> The major symptom is heat intolerance with hyperhidrosis of only the face and upper trunk. Hyperhidrosis in unaffected areas compensates for the inability of anhidrotic areas to



dissipate heat.<sup>29</sup> Occasionally, patients with anhidrosis have facial sweating while eating cheese, chocolate, or highly spiced foods or while drinking alcohol.<sup>30</sup> This phenomenon may be due to regenerating sudomotor nerve fibers aberrantly sprouting connections with gustatory secretomotor fibers.<sup>31</sup> The diagnosis of diabetic anhidrosis is readily made by covering the patient with quinizarin powder (which turns blue when moist) and exposing him to heat.<sup>29</sup> Therapeutically, patients can minimize compensatory hyperhidrosis by avoiding overheated environments. Gustatory hyperhidrosis may be minimized by avoiding specific foods that regularly produce this symptom. Patients with the latter problem may benefit from atropinic medications but frequently prefer to endure their symptoms rather than the side effects of the medication.

#### *Vasomotor Dysfunction*

Another autonomic abnormality that is demonstrably symmetric is vasomotor dysfunction.<sup>32</sup> Orthostatic hypotension may result from decreased sympathetic neural activity (efferent dysfunction seems most usual because of intact reflex tachycardia in most of these patients), from peripheral resistance to norepinephrine, or from a combination of these factors.<sup>33,34</sup> The prime symptom produced by these abnormalities is postural syncope, which occurs in 6 to 16% of patients with diabetic neuropathy.<sup>13,35</sup> Treatment with 9 $\alpha$ -fluorohydrocortisone and full-length fitted stockings is helpful.

#### *Painless Myocardial Infarction*

Autonomic neuropathy may also explain the increased incidence of painless myocardial infarction in diabetic patients.<sup>36,37</sup> The mortality rate is higher from painless myocardial infarctions than from painful coronary occlusions (47% versus 35%).<sup>35</sup> Therefore, unexplained cardiac failure or ketoacidosis in the diabetic patient should prompt a search for evidence of myocardial infarction.

#### *Neurogenic Bladder*

Another serious form of autonomic neuropathy is neurogenic bladder dysfunction — a condition that may predispose to urinary tract infection. This problem is present subclinically in as many as 87% of diabetic patients.<sup>38</sup> Neurogenic bladder dysfunction produces frank signs and symptoms in 14% of patients with clinical neuropathy.<sup>13</sup> The most common abnormality is loss of bladder sensation (due to neuropathic involvement of sympathetic afferents), causing detrusor atony. Less common abnormalities include

detrusor hyperreflexia and detrusor-internal sphincter dyssynergia (both due to corticospinal tract compromise). Segmental demyelination of the pudendal nerve occasionally causes sphincter paralysis in diabetic patients.<sup>39</sup>

Symptoms of detrusor atony include decreased urinary frequency — first manifested as remission of nocturia with voiding of large volumes in the morning. Disparity between increased glycosuria and improvement in the hyperglycemic symptom of polyuria should prompt investigation of bladder function. As detrusor atony worsens, the patient has difficulty initiating micturition and strains to compensate for weakness of the urinary stream. Postmicturition dribbling develops, and the patient becomes aware of the sensation of incomplete emptying of the bladder. Incomplete emptying may interfere with the accuracy of fractional glycosuria checks.<sup>40</sup> Severe detrusor atony may be associated with a massively enlarged bladder mimicking ascites or intra-abdominal tumor.<sup>41</sup> The patient may have overflow incontinence. Such decompensation of neurogenic bladder dysfunction is frequently precipitated by stress.<sup>40</sup>

Diagnosis is made by checking postvoid residual urine, performing cystometry, and examining the bladder cystoscopically for evidence of obstruction. Detrusor hyperreflexia should raise the question of spinal cord involvement by trauma or tumor or by vascular malformation. Tabes dorsalis characteristically causes detrusor hyporeflexia (like diabetes), and the possibility of tabes should be excluded in such patients.

Patients with mild disease should be urged to void every two or three hours despite the absence of the sensation of bladder fullness. With more severe involvement, contribution from prostatic hypertrophy should be sought and treated. Anticholinergic and  $\alpha$ -adrenergic medicines should be withdrawn if possible. Administration of bethanechol chloride, 50 to 75 mg every four hours by mouth, may be useful.<sup>41</sup>

Decompensated bladders (especially with accompanying infection) may require hospitalization for intermittent catheterization, antibiotic treatment of complicating infection, and subcutaneously administered bethanechol chloride, 5 to 10 mg every four hours. If the postvoid residual is less than 50 ml when low doses of bethanechol are parenterally administered, changing to oral medication is advisable. Manual pressure over the bladder (Credé's maneuver) is a useful adjunct. For resistant disease, phenoxybenzamine, 10 mg each day, can be added, with attention to possible development of orthostatic hypoten-



sion.<sup>42,43</sup> Persistence of bladder decompensation is an indication for transurethral bladder neck resection.

One of the side effects of phenoxybenzamine and of a transurethral bladder neck resection — retrograde ejaculation — may also result from autonomic neuropathy. Retrograde ejaculation is caused by neuropathy impairing the sympathetic efferents to the internal sphincter of the bladder neck. In this condition there is sensation of ejaculation without appearance of the ejaculate. The prime result is infertility — a sequela that may be treated by artificial insemination of sperm recovered by centrifugation of postmasturbation urine.<sup>44</sup> A recent report of successful treatment of this condition with bropheniramine is intriguing, and this modality merits further trials.<sup>45</sup> A potential complication of bropheniramine use is precipitation of bladder atony by the anticholinergic properties of the medication.

### *Impotence*

The occurrence of neurogenic bladder dysfunction in 82% of impotent diabetic males compared with its 10% incidence in potent diabetic males suggests a neuropathic cause for the impotence.<sup>46</sup> This neuropathy appears to affect primarily the nervi erigentes, the S<sub>2</sub>-S<sub>4</sub> parasympathetic efferents. Forty percent of impotent diabetic males have complete absence of the penile pulse on Doppler study and half of this latter group have signs of arterial disease in their legs.<sup>47</sup> Testosterone levels are normal in the overwhelming majority of impotent diabetic males.<sup>46,48</sup> Psychogenic factors, which produce more than 95% of impotence in the general population,<sup>49</sup> may be the sole cause of impotence in as few as 10% of impotent diabetic males.<sup>46</sup> Thus, the frequent occurrence of impotence in diabetic males (two to five times more frequent than the incidence in the general population)<sup>50</sup> seems to arise primarily from two organic causes — neuropathy and angiopathy.

Most impotent males note a gradual rather than a sudden loss of penile erection.<sup>46</sup> Symptoms of testosterone lack such as diminished beard and axillary hair growth are generally absent. Another symptom of testosterone lack — loss of libido — is not elicited at the time of loss of potency, but libido gradually diminishes thereafter in most of them.<sup>46,50</sup> Unlike the organic impotence of diabetes, in psychogenic impotence, morning erections continue to occur, impotence is periodic, masturbation is possible, and nocturnal emissions occur.<sup>46</sup>

Physical examination should include evaluation of the nervi erigentes by eliciting the bulbocavernosus reflex. The glans penis is squeezed, and reflex

contractions of the bulbocavernosus muscle is assessed by palpation. The status of the penile arteries can be examined by palpation of the pulses and by Doppler ultrasound technique. Examination of beard, body hair, and testicular and prostatic size is useful in evaluating testosterone status. Plasma testosterone level will supplement clinical findings.

If testosterone deficiency is documented, then hormone replacement may reverse the impotence. Such therapy is not helpful in patients with normal androgen levels.<sup>46</sup> Some of the vascular lesions producing impotence (such as Leriche syndrome) may be surgically correctable. If a neurogenic cause is documented, then the treatment of choice is surgical implantation of a penile prosthesis.<sup>51</sup>

### *Diabetic Enteropathy*

The 100% incidence of impotence and frequent occurrence of other autonomic neuropathies in diabetic enteropathy comprise the strongest evidence for a neurogenic cause of this enteropathy.<sup>46,52</sup> Pathologic study has not definitively localized the defect to the autonomic nervous system.<sup>53</sup> One biopsy study reported a spruelike mucosal atrophy (usually partial) in 33% of all diabetic males.<sup>54</sup> Increased coincidence of diabetes and celiac disease has been observed by some investigators.<sup>55</sup> However, the overwhelming majority of male patients with gastrointestinal dysfunction of diabetes do not respond to gluten restriction,<sup>56</sup> and this frequently observed mucosal atrophy may be an effect rather than a cause of the fundamental disturbance.<sup>57</sup> Mediation of diarrhea and steatorrhea by hypomotility-induced bacterial overgrowth is demonstrable in only 20% of patients.<sup>58</sup> Thus, while the fundamental disturbance that produces chronic diarrhea in 7% of all diabetic patients (compared with 2% of nondiabetic patients) may be autonomic neuropathy,<sup>59</sup> definitive evidence for this is not yet available.

Diabetic diarrhea is most common in patients between 20 and 40 years of age who have had diabetes for at least five years and have had poor diabetic control for months to years. Manifestations of sensory polyneuropathy, as well as autonomic neuropathy, are prominent.<sup>52,57</sup> Stools are profuse and watery rather than fatty. Urgency is common. It is sometimes associated with borborygmi and discomfort but rarely with pain. Fecal incontinence may be present, but patients usually have normal basal anal sphincter tone.<sup>57</sup> Diarrhea tends to occur after meals and at night. Symptomatic episodes may persist from hours to days (rarely months to years), and they tend to recur. After a bout of diarrhea, the patient may be constipated



for a period until normal bowel movements resume. Within five years, 90% of patients have either total remission or pronounced diminution in the frequency and severity of symptoms.<sup>52</sup> Despite steatorrhea in as many as 92% of patients with diabetic diarrhea,<sup>52</sup> signs and symptoms of vitamin deficiency states (tetany, osteomalacia, glossitis, bleeding diatheses) do not appear.<sup>60</sup> Extensive loss of weight and inanition are also distinctly uncommon.<sup>21</sup>

Laboratory studies show steatorrhea (excretion of 10 to 40% of the daily fat intake).<sup>52,57</sup> Levels of serum calcium, alkaline phosphatase, total protein, and carotene are normal (the carotene level being characteristically elevated in diabetes).<sup>57</sup> Hemoglobin levels are normal, and red blood cells are usually normocytic. Prothrombin time is normal, as is the excretion of xylose.<sup>21</sup> Spurious decrease in xylose excretion may arise from atony of stomach or bladder.<sup>57</sup> Barium contrast studies of the digestive tract show delayed gastric emptying in 30% of patients<sup>61</sup> and less commonly reveal small intestinal abnormalities such as thickened mucosal folds, dilatation of small-bowel loops, and a slowed transit time.<sup>52,57</sup> Secretion of pancreatic enzymes is normal.<sup>61</sup> Examination of jejunal biopsy specimens by the usual techniques shows normal mucosa.<sup>52</sup> These studies are indicated

because of the association of diabetes with exocrine pancreatic disease (especially pancreatitis) and with sprue.<sup>55</sup>

In the treatment of diabetic diarrhea, therapeutic success is difficult to document (because of the remitting nature of the condition) and is frequently elusive. The 20 to 50% of such patients who respond to treatment with tetracycline<sup>58,62</sup> tend to improve dramatically shortly after the first daily dose of 250 mg. Bethanechol chloride (0.5 mg subcutaneously every 8 hours after 15 mg orally every 8 hours) may be most useful in patients with demonstrable vagal hypofunction — for example, abnormal results on the Hollander test.<sup>63</sup> Symptomatic treatment with psyllium hydrophilic mucilloid and diphenoxylate hydrochloride, 20 mg each day, may be helpful.<sup>57</sup>

### Summary

The symmetric neuropathies of diabetes probably arise from metabolic injury to nerves and nerve sheaths. Sensory polyneuropathy can produce severe discomfort and may predispose to serious complications. This form of symmetric neuropathy may respond to improvement in diabetic control. The autonomic neuropathies are often difficult to control and require systematic approaches to diagnosis and treatment.

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Editor Emeritus



# Rheumatology Corner

## Role of Surgery in Rheumatoid Arthritis

R. VOLLERTSEN, M.D.\*

ALTHOUGH REST, PHYSICAL therapy, and anti-inflammatory agents are the initial treatment of rheumatoid arthritis, surgical therapy has an integral role in the management. The purpose of this article is to provide an overview of the surgical management of rheumatoid arthritis.

The major indication for surgery is relief of intractable pain, but a secondary improvement in function is often obtained. When functional improvement is the goal, the demands of the individual patient must be carefully considered if surgery is to be successful. Improvement in appearance is a relatively minor indication for surgery in the rheumatoid patient.

Synovectomy is one of the most controversial surgical procedures for rheumatoid arthritis. Synovectomy of the flexor and extensor tendons at the wrist is of value and is often combined with other procedures such as a carpal tunnel release if indicated. However, controlled studies have revealed no significant difference in symptoms or radiographic deterioration from metacarpophalangeal joint synovectomy. Similarly although synovectomy of the knee led to diminished swelling bony involvement progressed. It is felt that synovectomy can be effective in the local control of knee disease when performed before radiographic damage has occurred. This however is not a cure as the synovitis may reoccur in one to three years.

The development of foreign material for use in the human body has opened a new era in medicine. It has been said that the total hip arthroplasty is the most important reconstructive surgical advancement of the Twentieth Century and probably the greatest therapeutic advance ever for patients with rheumatoid arthritis. The prosthesis consists of a metal alloy and a high density polyethylene couple which is held in place with polymethylmethacrylate cement. A variety of models are now available and pain relief can be expected in 96 percent of cases. The major complications are infection and loosening. The incidence of late infection is increased in the rheumatoid patient and loosening is

especially likely to occur in the active patient.

The development of nonlinked total joint arthroplasty for use in the knee has provided greater than 80 percent pain relief with preservation of 90 degrees of motion. When stability is severely compromised at the knee, a hinge type of prosthesis is used. The complications of total knee arthroplasty are similar to those for total hip arthroplasty.

The experience with total joint arthroplasty has been much less at other joints, however, a total wrist arthroplasty has been recently advocated as preferable to arthrodesis at the wrist. The role of total arthroplasty is less clear at the metacarpophalangeal joints, metacarpotrapezial joint, elbow, ankle, and metatarsophalangeal joints, but may be beneficial in some cases.

Partial arthroplasty of the shoulder with humeral head resurfacing has been shown to relieve pain in 92 percent of cases with only a 2 percent mechanical failure rate. Although the main indication is persistent shoulder pain, abduction and internal rotation are significantly improved. Femoral head resurfacing and hemiarthroplasty at the knee are other partial arthroplasties currently being evaluated.

Successful arthrodesis of a joint provides pain relief and stability, but the loss of motion that is associated makes this a functionally unattractive alternative at some joints particularly the noninfected hip and knee. This may, however, be a very satisfactory procedure at other joints. A wrist arthrodesis may actually increase hand function by increasing the grip strength. Arthrodesis of the hand joints, particularly the first metacarpophalangeal and first interphalangeal joint can provide a stable pinch.

In conclusion, surgical therapy has an essential role in the management of the rheumatoid patient, chiefly in treating relatively localized pain which is unresponsive to conservative treatment. It is important that the physician be familiar with the special problems of the rheumatoid patient, the functional requirements and expectations of the individual patient, before any surgical procedure is undertaken.

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Product Information as of September, 1977  
U.S. Patent 2,985,558

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# Gerontology

## Minneapolis High Rise Nurse Program

A Study

DONNA MAE PETERSON\*

MINNEAPOLIS HAS THE highest percentage of older people of any major U.S. city: 20 per cent of the population is 60 or over.<sup>1</sup> Approximately 7 per cent of the older population (or 5400 people) live in the 42 high rise buildings sponsored by the Minneapolis Housing and Redevelopment Authority (MHRA) for low income elderly and handicapped people. The high rise residents are a high priority group for many health and social services in that they have low incomes, are older (one fourth are over 80), and are mostly single or widowed women who live alone.

A high rise nurse program sponsored by six hospitals and clinics (Lutheran Deaconess, Nicollet Clinic, Eitel, Metropolitan Medical Center, North Memorial, and Smiley's Point Clinic)† employs 16 RNs to provide on-site health services. The hospitals and clinics absorb the cost of the program which is offered free of charge to older people.

The 16 nurses offer their services on a scheduled, weekly basis, and spend from two to eight hours at each site. Clients need not make appointments; they can go to the nurse's office area or be visited by the RN in their apartments.

There is no definitive, written description of the high rise nurse program. The United Way of Minneapolis Area conducted a study to determine who the nurses served, what services were offered to clients, and what the nurses' perceptions of the program were.

### Method

A sample of eight clients of each nurse was randomly selected from a list of all clients the RNs had seen on the day prior to the interview. Complete information was obtained on all 128 clients in the sample. To ensure confidentiality, the interviewer asked all questions of the nurses and never saw client names or records.

Each nurse was also asked to fill out a questionnaire which was designed to obtain information on the nurse's attitudes and perceptions. All 16 nurses returned completed questionnaires.

\*Research Associate, United Way of Minneapolis Area. Copies of the complete report can be obtained from the United Way, 404 South 8th Street, Minneapolis, 55404 or call 340-7593.

†The number of nurses from each sponsor is: Metro Medical Center (5), North Memorial (4), Lutheran Deaconess (3), Smiley's Point (2), Nicollet Clinic (1), and Eitel (1); since August of 1978, Nicollet is no longer in the program.

### Findings

#### *Demand*

There is a high demand for the high rise nurse service. Nurses spend an average of just eight-and-a-half minutes with each client, which is partly a result of the demand for the service relative to the supply of RN time. Most clients use the service repeatedly, coming on a weekly or biweekly basis. Because health problems tend to increase with age, the demand for the nurse's service is relatively constant among existing clients. Eighty per cent of the clients have used the service for at least one-to-two years; one-third have used it for at least three years.

The clients appear to be satisfied with the service in that most use it repeatedly, most follow the RN's advice, and most were judged by the nurses as being pleased with the service.

Eighty-five per cent of the clients came to the nurses at their "offices". Thirteen per cent were visited by the nurses in their apartments; 2 per cent were seen in a hospital or nursing home.

#### *Contact with Medical Care System*

Clients of the high rise nurses are connected with the medical care system. Ninety per cent had seen a physician in the past year, and nearly half had seen one in the past month. Data from other local studies on visits to physicians indicates that this is high.<sup>2</sup>

TABLE 1  
Last Time RN Client Saw Physician

	Per Cent (N=128)	Cumulative Per Cent
Less than 1 month	45	45
2-3 months	25	70
4-6 months	14	84
7-12 months	6	90
1-2 years	2	92
Don't know	8	100

If the cases where the nurse did not know this information are omitted, 97 per cent of all RN clients had seen a physician in the past 12 months. All the RN clients who had been to a physician in the past year had seen a general practitioner or internist, and one-fourth had also seen an M.D. specialist.

RN clients are not seeing physicians for treatment of



health problems only: three-fourths had had a physical within the past year, and for most of the remaining clients, the nurse did not know.

**TABLE 2**  
**Last Time RN Client Had Physical**

	<b>Per Cent (N=127)</b>	<b>Cumulative Per Cent</b>
Less than 1 month	19	19
2-3 months	21	40
4-6 months	16	56
7-12 months	18	74
Over 1 year	2	76
Don't know	24	100

Thirty per cent of the RN clients had been hospitalized within the past year. This may indicate that the nurses are serving persons with serious health problems. The cause and effect of older persons being in recent contact with a physician or being hospitalized and also being clients of the RNs is not known. One possible explanation is that persons who regularly see physicians are more likely to be conscious of their health and avail themselves of the nurses' services. An alternative explanation is that the nurses encourage the clients to see their physicians, and therefore increase the chances that these older people have done so. There were indications in the nurses' descriptions of services offered that such encouragement is very common.

#### *Client Problems*

The most common problems among RN clients were cardio/cerebrovascular and mental/emotional. The nurses were asked what each client's major or prevailing health problems were that had come to her attention. This information was coded into 12 categories based on those used in Dr. Robert Derro's St. Paul High Rise Clinic study.<sup>3</sup> Eighty per cent of the clients had cardio/cerebrovascular problems. The second most common problem was mental/emotional with half the clients experiencing this kind of problem.

Physical and mental/emotional problems existed side by side for half the RN clients. Only one client judged as having a mental/emotional problem did not also have a physical problem. Physical health problems and the resulting disabilities may partly explain the high incidence of mental health problems among these older people but there are other factors associated with aging, such as loss of spouse, retirement, reduced income, and isolation from younger people that are also probable causes of depression among older people. Table 3 shows client problems classified by functional system.

Over 40 subcategories were developed within the 12 major problem categories. Problems common to 3 per cent or more of the clients are shown in Table 4.

**TABLE 3**  
**RN Client Major Problems by Functional System\***  
**(Total clients = 128, total problems = 312)**

	<b>Per Cent of Clients</b>
Cardio- and cerebrovascular	80
Mental/emotional	48
Musculoskeletal	31
Endocrine, nutritional, metabolic	27
Nervous system and sense organs	12
Digestive	12
Genitourinary and gynecological	7
Side effects of medication	7
Respiratory	6
Signs, symptoms, and ill defined conditions	6
Blood and blood forming organs	5
Skin and subcutaneous	3

\*The following qualifications apply to the data in Tables 3 and 4: (1) only current problems were recorded; (2) only problems which had come to the nurse's attention were recorded; and (3) the interpretation of "major or prevailing" problem undoubtedly varied from nurse-to-nurse.

The most common specific problem was hypertension with half of all RN clients having this condition. Forty per cent of the RN clients suffered from depression. (Depression included loneliness, anxiety, fear, and sadness, but not more severe disorders such as psychosis, confusion, and disorientation.)

Cardio- and cerebrovascular impairments were problems for 29 per cent of the clients. Examples of conditions classified in this category are strokes, arteriosclerotic heart disease, heart attacks, congestive heart failure, and aneurysms.

**TABLE 4**  
**Major Specific Problems\***  
**(Total clients = 128, total problems = 312)**

	<b>Per Cent of Clients</b>
(1b) Hypertension	49
(11c) Depression	40
(1a) Cardio- and cerebrovascular impairments	29
(7b) Arthritis/Inflammatory problems	26
(2c) Weight (over or under)	16
(4a,6a,7a,9a) Cancer	7
(12) Effects of medication	7
(2b) Diabetes	6
(11b) Confusion/disorientation	6
(5b) Vision problems	6
(2a) Thyroid	4
(7c) Trauma/degeneration (musculoskeletal)	4
(6b) Herniation	3
(5c) Hearing loss	3
(9b) Anemia	3



### *Referrals*

The primary referral role of the nurses was in advising clients as to whether or not they needed to see their doctors. Of the 23 clients (or 18 per cent) who were referred on the previous day, all but one already had a physician. Thus, the nurses do not need to help most clients find a physician, but rather provide advice or encouragement for them to see their existing physician.

The role of the nurses in referring clients back to their physicians is sometimes initiated by the physicians who ask the nurses to refer the client if there are changes in a known condition. In other instances, the clients use the RNs on their own as advisors in deciding whether or not they need to go to their doctors. This advisory function can be particularly important to older persons in high rises who are likely to encounter a number of barriers in getting to the doctor's office. Accessing and paying for transportation, personal mobility restrictions, and insecurity are problems frequently faced by older people, particularly those who are very old and have a low income.

### *Barriers to Clients Obtaining Medical Care*

Costs not covered by Medicare was named by 15 of

the 16 nurses as a barrier to clients getting needed medical care. Other financial barriers identified by the nurses were: a) the physicians' charges exceed what Medicare will cover; b) the older person is not covered by Medicare or Medical Assistance\*; and c) the complex forms and procedures for reimbursement by Medicare or Medical Assistance discourage people from seeking care.

Client based problems were also identified as barriers to older people obtaining needed medical care. Thirteen nurses named client fears as a barrier, and 12 nurses said the clients' refusals to admit the problem were a barrier.

### **Acknowledgments**

A Task Force established by the United Way Health Committee determined the need for the study and guided the effort to completion. The Task Force Chairman was Fred Nimtz, Director of Social Services, Senior Citizen Centers; Vice Chairman was Thomas Hoban, Executive Vice President, Hennepin County Medical Society. Members were: Gudrun Stenoien, RN, Lutheran Deaconess Hospital; Katy Boone, Health Educator, Minneapolis Health Department; Sandra DuVander, Health Planner, United Way of Minneapolis; John Rafferty, Aging Planner, United Way of Minneapolis; Donna (Rortvedt) Peterson, Research Associate, United Way of Minneapolis.

Marilyn Klug, from Senior Citizen Centers, worked on all phases of the study. Katy Boone, from the Minneapolis Health Department, assisted with the conceptualization of the effort. Jean Desenclos was responsible for data coding and processing. Shirley Conn provided general consultation and assisted with the categorization.

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# Unsuccessful Pregnancy

## Protocol for Management of Unsuccessful Pregnancy

JANE E. HODGSON, M.D.\* and GORDON M. DITMANSON, M.D.\*

The term "unsuccessful pregnancy" is used to include intrauterine fetal death, missed abortion, gross fetal abnormalities, and hydatidiform mole. Successful management of 21 such cases is reported, and their complications discussed.

The need for active management of this common problem is identified and a protocol is described wherein dilatation and evacuation (D&E) is employed for gestations from 12 to 18 weeks' size, and prostaglandin induction for those gestations greater than 18 weeks' size. A preference is indicated for continuous extra-amniotic infusion of PGF<sub>2</sub> $\alpha$  over PGE<sub>2</sub> suppositories. A rationale for the salient additions to the protocol — laminaria tents, curettage, and prophylactic antibiotics — is presented. Outpatient management is advocated whenever possible.

THE TERM "unsuccessful pregnancy" includes intrauterine fetal death (IUFD), missed abortion, gross fetal abnormalities and hydatidiform mole. Although expectant management has heretofore been the treatment of choice, the recent availability of prostaglandins and newer abortion techniques have made active management a superior alternative in the treatment of this obstetrical problem.

Complications of expectant management are: (1) consumptive coagulopathy and hypofibrinogenemia which have been observed in as many as 40% of patients with IUFD,<sup>1</sup> (2) infection of the necrotic uterine contents with serious acute and chronic sequelae, and (3) the psychological trauma and

inconvenience of having to carry a dead or malformed fetus for an indefinite length of time.

The former use of hysterotomy in the management of these cases is no longer acceptable. Similarly, the use of intra-amniotic hypertonic saline carries the risk of possible hyponatremia or diffuse intravascular coagulopathy. The only other alternative to these problems has been oxytocin induction with or without amniotomy, which treatment is frequently inadequate because of (1) lack of uterine responsiveness to oxytocins, especially in the middle trimester, and (2) the generally unfavorable nature of the cervix.

A number of reports have recently appeared wherein prostaglandins have been utilized to terminate unsuccessful pregnancies<sup>2-8</sup>. Using continuous extraovular prostaglandin F<sub>2</sub> $\alpha$  infusion or prostaglandin E<sub>2</sub> sup-

\*Fertility Control Clinic, St. Paul-Ramsey Hospital, St. Paul, Minnesota.

TABLE 1

### Protocol for Management of Pregnancy Termination

Uterine size (weeks of gestation)	Diagnosis	Method of treatment
6-12 wk	A. Normal pregnancy	suction curettage
	B. Unsuccessful pregnancy	
	1. Missed abortion	suction curettage
	2. Hydatidiform mole	suction curettage plus sharp curettage
12-18 wk	A. Normal pregnancy	laminaria, D&E, and oxytocin
	B. Unsuccessful pregnancy	
	1. Molar pregnancy	laminaria, suction curettage and oxytocin plus sharp curettage.
	2. Missed abortion	laminaria, D&E, and oxytocin
	3. Defective fetus	laminaria, D&E, and oxytocin
≥ 18 wk	A. Normal pregnancy	laminaria, extraamniotic PGF <sub>2</sub> $\alpha$ and oxytocin
	B. Unsuccessful pregnancy	
	1. Fetal death in utero	laminaria, PGE <sub>2</sub> suppositories & oxytocin
	2. Defective fetus	laminaria, extraamniotic PGF <sub>2</sub> $\alpha$ and oxytocin
	3. Molar pregnancy	laminaria, suction curettage and oxytocin



positories, safe and effective alternatives to oxytocin induction and/or amniotomy have been developed. While authors have differed regarding augmentation of medically induced labor with oxytocin or laminaria tents, none have heretofore reported the elective use of dilatation and evacuation (D&E) procedures except in cases of hydatidiform mole or when prostaglandin induction has failed. Neither has the use of extraamniotic  $\text{PGF}_2\alpha$  been popularized, in this country at least, for the treatment of unsuccessful pregnancy.

This paper reviews our experience with 21 cases of unsuccessful pregnancies referred to the Fertility Control Clinic at St. Paul-Ramsey Medical Center for active management between 8-17-75 and 6-1-78. In addition to emphasizing the advantages of aggressive treatment, the proper selection or management method for each type of case is outlined (Table 1).

### Materials and Methods

There were seventeen cases of IUFD, one molar pregnancy, and three cases of gross fetal defects, the latter including a case of anencephaly (28 weeks), a trisomy x (25 weeks) and an agenesis of the fetal urethra with bilateral polycystic kidneys (20 weeks). Duration of amenorrhea ranged from 12 to 31 weeks.

The choice of procedure (Table 1) for termination of the pregnancy is determined by uterine size rather than by the gestational age as calculated by the length of amenorrhea. Ultrasonography to determine fetal biparietal diameter (BPD) and presence of fetal activity is an additional aid in diagnosis. Uteri of 12 to 18 weeks' size are usually evacuated by the use of laminaria and dilatation and evacuation (D&E). Patients with uteri larger than 18 weeks' size are treated with laminaria,  $\text{PGF}_2\alpha$  continuous extraamniotic infusion or  $\text{PGE}_2$  suppositories, plus oxytocin augmentation (with the exception of hydatidiform moles which are best treated with suction curettage regardless of uterine size).

Laboratory evaluation includes coagulation profile, hemogram, blood group and Rh type, urinalysis, cervical culture for *Neisseria gonorrhoeae*, VDRL and a Papanicolaou smear.

#### D&E

In the afternoon preceding surgery one to eleven laminaria tents are inserted into the cervical canal and the patient is allowed to return home or to a nearby motel. Approximately sixteen hours later, the patient returns for removal of the laminaria and the uterine evacuation (D&E) as an outpatient surgical procedure under general anesthesia. Methylergonovine maleate 0.2 mg is given intravenously immediately prior to

evacuation, and oxytocin (40 U/liter of Ringer's lactate) is maintained throughout the procedure and for two hours in the recovery room until patient is discharged.

#### Extraamniotic $\text{PGF}_2\alpha$ Continuous Infusion

If the uterine size exceeds an 18 week gestation or the biparietal diameter is greater than 4.0 cm by ultrasonography, extraamniotic  $\text{PGF}_2\alpha$  is employed. As many laminaria tents as possible (one to 11) are inserted into the cervical canal in the afternoon prior to induction. The technique of utilizing the extraamniotic route by continuous infusion of  $\text{PGF}_2\alpha$  by means of a 30 cc Foley bag catheter and a constant infusion pump after insertion and removal of intracervical laminaria tents has been described in a previous publication.<sup>9</sup>

Oxytocin augmentation is begun when the Foley bag is expelled or when it becomes palpable at the internal os, along with the establishment of a good labor pattern. Intravenous oxytocin, 10 U/hr/100 ml of Ringer's lactate, equivalent to a rate of  $167\mu\text{ U/min}$ , is usually necessary because of the lack of sensitivity of the midtrimester uterus to lower doses. The careful monitoring of intake and output and serum electrolytes is necessary for prevention of water intoxication which may result from the antidiuretic effect of oxytocin.

Following delivery of the fetus, meperidine and/or diazepam are given intravenously for analgesia during recovery of the placenta. Although delivery may be spontaneous, immediate, and apparently complete, routine uterine exploration and inspection of the cervix is mandatory. In the event of cervical lacerations immediate and careful repair should be performed. General anesthesia is rarely required. Intravenous oxytocin is continued for two hours following delivery at  $167\mu\text{ U/min}$  to avoid uterine atony. The patient is usually discharged shortly thereafter.

### Results

In each of the 21 patients the pregnancy was successfully terminated without complication except for two patients requiring transfusion for blood replacement. There were no cases of endometritis, uterine perforation, laparotomy, hysterotomy, hysterectomy, or cervical injury. As all patients underwent routine uterine exploration and cervical inspection according to the protocol, such procedure was not considered a complication.

#### D&E (Table 2)

Six patients underwent dilatation and evacuation under general anesthesia. Their gestations ranged from 14 to 18 weeks. An average of 3.8 laminaria tents were



used. The only complication occurring in this group was in the case of a 14-year-old girl with a 18 week molar pregnancy. Hemoglobin determination on admission was 10.0 grams. Due to rather excessive preoperative bleeding she received four units of whole blood. Estimated blood loss during surgery did not exceed 250 cc. Her postoperative recovery was rapid and uneventful.

#### *PGF<sub>2</sub>α (Extraamniotic)*

Eight patients underwent laminaria insertion and removal followed by extraamniotic prostaglandin F<sub>2</sub>α induction with oxytocin augmentation. Six of these were cases of IUFD ranging from 12 to 28 weeks' uterine size. Induction abortion time\* averaged 11.5 hours. The remaining two patients were diagnosed as having a grossly defective fetus (anencephaly and a trisomy X). The greater ease of induction in IUFD as compared to anomalous pregnancies is demonstrated by the longer IAT in the latter two patients (21.5 hours).

One of the earliest procedures in this group was performed on a patient who was 18 menstrual weeks pregnant by dates. Her progress with extraamniotic PGF<sub>2</sub>α was slow and a surgical (D&E) was performed after 36 hours, revealing necrotic products of conception not greater than 12 weeks' duration. This was an obvious error in choice of method due to the fact that the decision was based upon menstrual history rather than uterine size. This case supports the argument for

using D&E in cases of IUFD when uterine size is less than 18 weeks. The only complication in the extraamniotic PGF<sub>2</sub>α group occurred with an infertility patient, an elderly 41-year-old primigravida with a myomatous uterus and a 25 week pregnancy (trisomy X). Her induction abortion time was 34.5 hours. Delivery was followed by a 1000 cc hemorrhage due to uterine atony during curettage for recovery of the placenta. After receiving a transfusion of two units of whole blood, recovery was uneventful.

#### *PGE<sub>2</sub> Suppositories*

20 mg suppositories of prostaglandin E<sub>2</sub>† first became available in November of 1977 for use in the treatment of fetal death in utero and missed abortion. These frozen suppositories are placed one at a time high in the posterior vaginal fornix at intervals of three to five hours. The patient remains supine for at least ten minutes, but is otherwise not restricted and can be ambulatory during most of the treatment.

Four patients with IUFD underwent induction with PGE<sub>2</sub> (20 mg) suppositories. Uterine sizes ranged from 20 to 31 weeks. An average of 4 laminaria tents (range 0 to 8) were used and induction abortion time averaged 4.5 hours with no more than two PGE<sub>2</sub> suppositories required for each case.

One patient with an anencephalic pregnancy of 31 weeks initially underwent induction with extraamniotic PGF<sub>2</sub>α. Spontaneous rupture of the membranes occurred early with sufficient dilatation of the cervix to prohibit the use of a Foley catheter and the induction was continued with 4 (20 mg) PGE<sub>2</sub> suppositories and oxytocin. She experienced nausea and vomiting with both types of prostaglandin and her temperature

\*Induction abortion time (IAT) is defined as the time from the initial extraamniotic instillation of PGF<sub>2</sub>α to the expulsion of the fetus.

†Prostin E<sub>2</sub> — The Upjohn Company, 7000 Portage Road, Kalamazoo, Michigan.

**TABLE 2**  
**Treatment and Results in 21 Cases of Unsuccessful Pregnancy**

Type of Procedure	Diagnosis	Number of Patients	Average Uterine Size (Weeks)	Number of Laminaria	Average Induction Abortion Time (hr)
1. Laminaria & D&E	IUFD	5	14.4	3.8	
	Mole	1	18		
2. Laminaria & PGF <sub>2</sub> α & Oxytocin	IUFD	6	21	3.8	11.5 (6.8-20)
	Defective Fetus	2	22	5.5	21.5 (8.5-34.5)
3. Laminaria & PGE <sub>2</sub> Suppositories & Oxytocin	IUFD	4	26.2	4	4.5 (2.5-6.8)
4. Laminaria & PGF <sub>2</sub> α & PGE <sub>2</sub> & Oxytocin	Defective Fetus	1	31	6	32
5. Laminaria & Oxytocin	IUFD	2	22.5	1.5	6.7 (5.5-8)



reached 101°F. Fever promptly subsided following discontinuance of the drug. The induction was otherwise uncomplicated, but required thirty-two hours.

The side effects of both  $\text{PGF}_{2a}$  and  $\text{PGE}_2$  are nausea and vomiting, diarrhea and hyperthermia. They are usually transitory in character and subside promptly with discontinuance of the drug.

Two patients with IUFD with gestations of 22 and 23 weeks, were successfully delivered following the use of laminaria and oxytocin alone, with IATs of 5.5 and 8 hours. Mild contractions developed following the insertion of laminaria tents and labor progressed to delivery with oxytocin alone.

### Discussion

Calder and his associates,<sup>2</sup> reporting a series of cases of IUFD treated with extraamniotic  $\text{PGF}_{2a}$  stated that surgical intervention from 12 to 17 weeks was more "hazardous" than extraamniotic prostaglandin induction, although the latter took longer than D&E. Our experience with D&E has not confirmed Calder's opinion but has tended to support the findings reported by Grimes<sup>10</sup> in 1977 that the rates of endometritis, retained products of conception and hemorrhage are significantly less with D&E than with medically induced abortion in the early midtrimester up to 18 weeks. Although the risk of cervical injury is reportedly greater with D&E, according to Grimes, it is our opinion that the routine use of laminaria tents pre-operatively essentially eliminates this complication. However, it is the authors' opinion that surgical evacuation is usually contraindicated when the uterine size exceeds 18 weeks except where medical induction has failed.

#### *Extraamniotic Prostaglandin $F_{2a}$ versus Prostaglandin $E_2$ Vaginal Suppositories*

Initially hailed with much enthusiasm, the prostaglandin  $E_2$  suppositories, though simple to administer, have several distinct disadvantages when compared with continuous extra-amniotic infusion of  $\text{PGF}_{2a}$ . With the latter method, a continuous sustained effect is achieved with a smaller dose, whereas the suppositories provide an intermittent prostaglandin effect which is dependent upon systemic absorption of higher doses of the drug. Therefore, side effects are usually greater with the  $\text{PGE}_2$  suppositories than with the extraamniotic continuous infusion of  $\text{PGF}_{2a}$ . Vaginal absorption of any drug is variable and its administration via a vaginal suppository cannot be controlled as easily as by the continuous infusion

pump. Furthermore the leukocytosis and hyperthermia more frequently invoked by  $\text{PGE}_2$ , than by  $\text{PGF}_{2a}$  may obscure the diagnosis or a true infection. Another advantage of the extraamniotic  $\text{PGF}_{2a}$  is the pressure of the Foley bag which facilitates cervical dilatation. This effect is not dependent upon intact membranes.

A theoretical disadvantage of continuous infusion of  $\text{PGF}_{2a}$  is risk of infection with an indwelling catheter. Fears of sepsis after intrauterine administration of prostaglandins have not materialized in the experience of most investigators however.<sup>11</sup>

The main advantage with the use of  $\text{PGE}_2$  suppositories is simplicity. Except for a short period of necessary recumbency, the patient may remain ambulatory. It is apparent that the use of  $\text{PGE}_2$  suppositories is limited to cases of IUFD where labors tend to be short and are more easily "triggered". Finally, the suppositories may be used to hasten delivery if excessive cervical dilatation precludes use of the Foley catheter in a case of arrested labor. The long term stability of  $\text{PGE}_2$  compounds in vaginal formulations is in some doubt and further evaluation is required.

#### *Routine Curettage*

Even though the products of conception appear to have been delivered spontaneously and completely following a prostaglandin induction the patient should undergo an immediate uterine exploration and curettage, usually with the aid of intravenous meperidine and diazepam. The added procedure requires but a few minutes and is usually justified by the amount of placental tissue recovered despite the "complete" appearance of the already delivered placenta. Although routine and immediate "prophylactic" curettage reduces subsequent complications, some authors perform curettage only after two, four, or eight hour waits for spontaneous expulsion of the placenta. Such variations in technique influence complication rates, such as endometritis and hemorrhage, rendering invalid comparisons of complication quoted by different authors.

#### *Prophylactic Antibiotics*

Routine prophylactic antibiotics are employed prior to any invasion of the uterus or cervix. Prophylactic antibiotics have been demonstrated to reduce complications and number of days of hospitalization following first trimester abortions<sup>12</sup> and similar benefits should be expected in second trimester terminations where incidence of endometritis may be as high as 8.1%<sup>13</sup>. The utilization of adjunctive measures such as immediate curettage in addition to



prophylactic antibiotics is important in avoiding post-abortion endometritis.

#### *Inpatient versus Outpatient*

Since January, 1978, all of the previously described services are available on an outpatient basis except where pre-existing medical complications may necessitate hospitalization. Laminaria tents are inserted in the clinic the afternoon preceding the induction and the patient is allowed to return to her home or a nearby motel over night. Medical induction or D&E is performed the next morning on an outpatient basis and the patient is discharged later that day in at least 90% of

the cases. Clinic closing hours may be delayed on occasion but this kind of flexibility is far more economical and satisfactory to the patient than is routine hospital admission.

The new concept of aggressive management of the unsuccessful pregnancy is worthy of emphasis as is also the proper selection of method of termination. All uteri under 14 weeks' size are best evacuated by suction curettage; 14 to 18 weeks' size by laminaria and D&E and over 18 weeks' size, by laminaria tents and either extraamniotic PGF<sub>2a</sub> or PGE<sub>2</sub> suppositories augmented by oxytocin.

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# Fracture Conference

## Fractures through Nonossifying Fibromata in Children

HAMLET A. PETERSON, M.D.\* and EDWARD M. FITZGERALD, M.D.†

### Case 1

**Dr. Edward H. Fitzgerald:** The first case this morning concerns a boy, age 12 years and 10 months, whose right leg gave way as he was running around second base during a baseball game. He sustained this injury (Figures 1 A and B).

**Dr. Hamlet A. Peterson:** Dr. Landon, would you comment on the history and Xray?

**Dr. Glenn C. Landon:** The Xray shows a pathologic fracture of the distal tibia and fibula with a large cystic area of sclerotic border.

**Dr. Peterson:** What might this lesion be?

**Dr. Landon:** From the Xray, it appears that it is a metaphyseal fibrous defect.

**Dr. Peterson:** Is this a common lesion?

**Dr. Landon:** Yes. Most are asymptomatic, and only large ones are likely to result in fracture.

**Dr. Peterson:** Is there any other lesion it might be?

**Dr. Landon:** A simple cyst.

**Dr. Peterson:** Anything else? Giant cell tumor?

**Dr. Landon:** No, not in this age group and not in this location.

**Dr. Peterson:** How might this fracture be managed?

**Dr. Landon:** The open wound would require debridement. While that is being done, I suppose some tissue should be obtained for biopsy. This lesion won't heal on its own, but you could speed healing by curettage with or without bone grafting. I wouldn't want to do the bone grafting now, because of the open wound.

**Dr. Peterson:** The fracture was difficult to reduce, mainly because the bone had punctured the skin and a larger incision was necessary for reduction. This was the pathologic specimen (Figure 2). Would you like to comment on it?

**Dr. Landon:** This is a typical nonossifying fibroma, with occasional benign giant cells scattered throughout.

**Dr. Peterson:** Note the cell-rich fibroblastic tissue disposed in somewhat whorled bundles. Sometimes

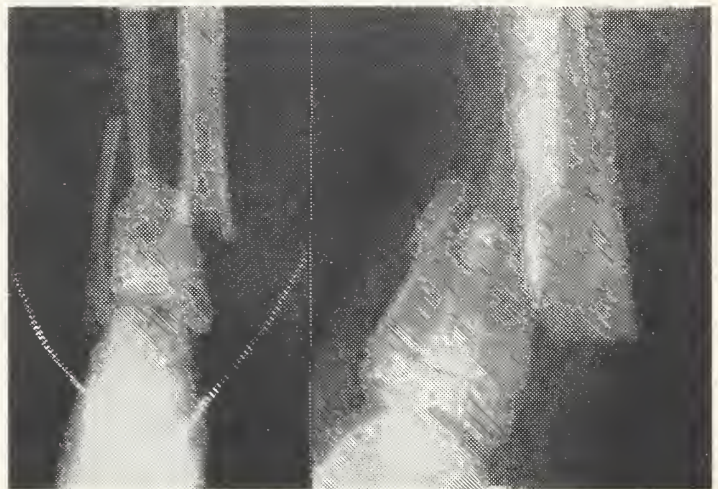


Fig. 1 (Case 1) — Open pathologic fracture through distal right tibia and fibula. (A-left) Anteroposterior view. (B-right) Lateral view.

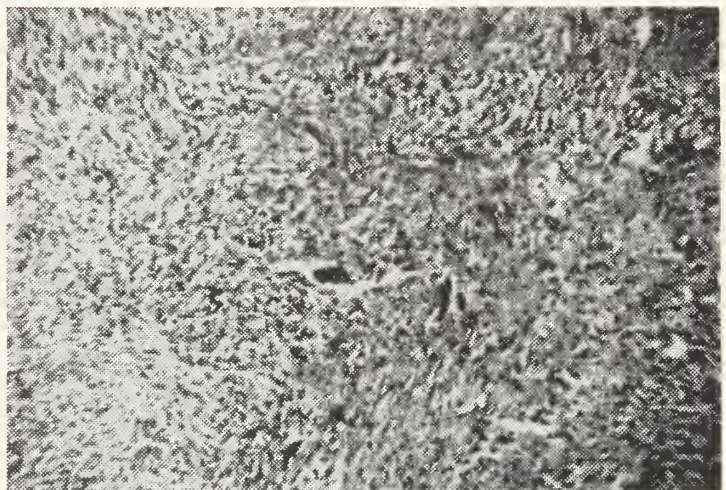


Fig. 2 (Case 1) — Tissue curetted from lesion at time of wound debridement. (Hematoxylin and eosin; x 100.)

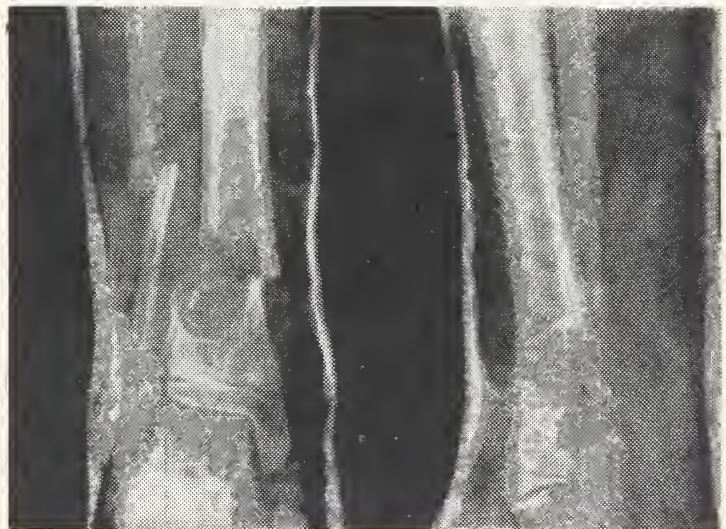


Fig. 3 (Case 1) — Position of fracture fragments after wound closure and casting. (A-left) Anteroposterior view. (B-right) Lateral view.

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these are also present with large lipophages. Hemosiderin pigmentation may be seen in the cytoplasm of the fibroblasts. We did as you suggested and curetted the lesion. Bone grafts were not added, because this open wound was contaminated. The wound was packed open. A delayed primary closure was performed after about a week, when the swelling had diminished. A cast was applied (Figures 3 A and B). Is this position and alignment adequate?

**Dr. Landon:** There seems to be slight valgus and angulation at the ankle which should be corrected.

**Dr. Peterson:** The cast was wedged to correct the alignment. What would you tell the parents about the rate of healing or the possibility of nonhealing through a large lesion like this or about possible future curettage and bone grafting?

**Dr. Landon:** I think one might expect slow healing, and evidence of this large lesion probably would persist on Xray for several years, but I think the probability of healing is high.

**Dr. Fitzgerald:** At four months, the cast was removed. Gradual motion and weight bearing were begun. Fourteen months after the injury, there was some ossification beginning in the lesion, which remained fairly sizable. The growth arrest line revealed even growth distally, so there was no damage to any part of the physis. Thus, varus or valgus won't develop from injury to the growth plate. As the growth plate moves away and the tibia becomes more tubular, the natural remodeling seems to devour the lesion. This is how most of the lesions disappear. As the bone becomes tubularized, these lesions, which are usually on the edge of the metaphysis, seem to get resorbed and replaced. However, some of the lesions will just ossify, as is illustrated in this case.

**Dr. Peterson:** Dr. Landon has called this a "metaphyseal fibrous defect." Are there any synonyms used for this lesion, Dr. Wertzberger?

**Dr. Kenneth L. Wertzberger:** "Nonossifying fibroma."

**Dr. Peterson:** Is there any distinction between these two, or are they completely synonymous?

**Dr. Wertzberger:** They're synonymous as far as pathology is concerned.

**Dr. Peterson:** Most people do regard them as synonymous. Some authors make a differentiation in size, calling the smaller lesions "metaphyseal fibrous defects" and the larger ones "nonossifying fibromas." This one is thus a nonossifying fibroma. Is there such a thing as an ossifying fibroma?

**Dr. Brian T. Briggs:** I don't know. Maybe this is ossifying.

**Dr. Peterson:** Fibrous dysplasia has many similar histologic features and, except for trabecular ossification, may be difficult to distinguish from nonossifying fibroma. Roentgenographically, small areas of fibrous dysplasia may also be difficult to distinguish from large nonossifying fibromata.

**Dr. Fitzgerald:** This patient was seen two years from the time of injury, and, as you can see, the lesion had ossified even more (Figures 4 A and B). There is one small lytic area. This time a scanogram was obtained. The involved leg was only 3 mm longer, so we were satisfied that a clinically evident discrepancy in leg length would not develop.

**Dr. Peterson:** If this boy would like to be active athletically, what is the potential for another fracture, or should some consideration be given to bone grafting? The parents were told at the time of injury that it would probably be necessary to bone graft it later. What do you think, Dr. Kearney?

**Dr. Michael M. Kearney:** These lesions have a tendency to disappear as the child matures, and that one doesn't look too bad. The cortex is a little thin. I would temporize.

**Dr. Peterson:** Would you let him play football?

**Dr. Kearney:** How old is he?

**Dr. Peterson:** Fourteen now.

**Dr. Kearney:** I would tell him that the Xrays suggest that the bone is a little weaker and that he might have a slightly increased risk of refracture. I would leave it up to him.

**Dr. Peterson:** I released him to all activities. Dr. Bianco, what is your opinion on this point?

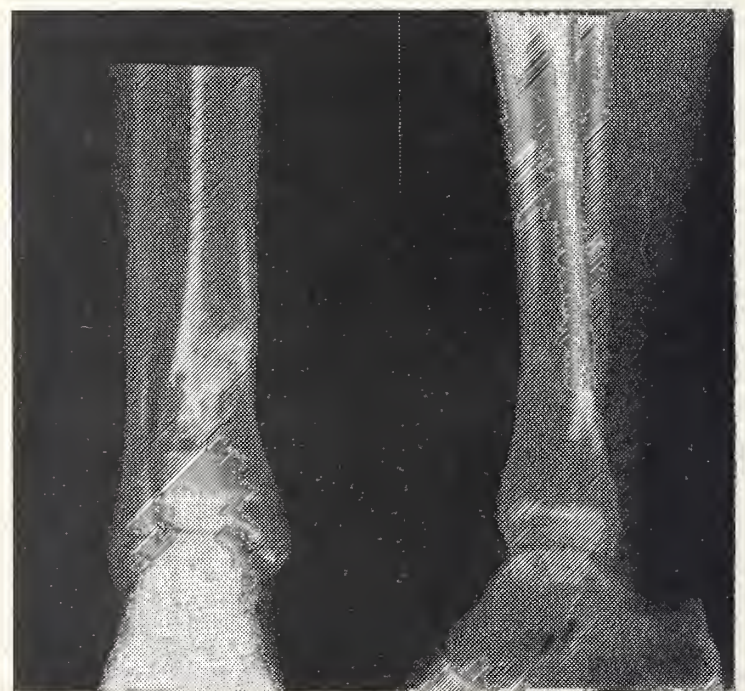


Fig. 4 (Case 1). Two years after injury. Age 14 years and 11 months. (A-left) Anteroposterior view (B-right) Lateral view.



**Dr. Bianco:** I think the bone is strong. I would let him play.

**Dr. Peterson:** Dr. Coventry, how do you feel about it? Would you let him play hockey?

**Dr. Mark B. Coventry:** Yes. I think hockey is less stressful on this than football. I wouldn't let him play football. I don't know how strong the bone is. It doesn't look perfect, but maybe it's stronger than we think. Perhaps Dr. Chao can devise some method to tell us how strong this is. Little torsion forces that we can't predict might break this, whereas a direct blow might not. It's all so nebulous. I would like to find some way of really knowing.

**Dr. Peterson:** Dr. Chao, can you tell us?

**Dr. Edmund Y. S. Chao:** Yesterday, Dr. Stephen Perren said that he and his colleagues have some way of scaling the gray density on Xray film according to the bone mineral contents to estimate bone stress.<sup>1</sup> It is an interesting concept, but he told us that this method is not very reliable, since bone density and strength are not closely correlated and the quality of Xray film would also affect the result. People have tried using a vibration method by tapping the bone and then detecting the quality of sonic wave passing through the fracture site to estimate the healing strength.<sup>2-4</sup> Soft tissue often creates artifacts to make this method less reliable. However, with future development it may become a valuable means to estimate in vivo bone strength.

## Case 2

**Dr. Fitzgerald:** The next case involves a boy 11 years and nine months old who was struck on the side of his right leg while playing football. Here is an Xray (Figure 5).

**Dr. Peterson:** Dr. Hartz, will you comment on this Xray?

**Dr. Charles R. Hartz:** It shows a rather displaced supercondylar metaphyseal fracture of the distal femur. Was his neurovascular status intact?

**Dr. Fitzgerald:** Yes.

**Dr. Hartz:** It looks as if there is a defect in the metaphysis. It looks like a fibrous cortical defect, probably benign.

**Dr. Fitzgerald:** Would you open this fracture to biopsy it?

**Dr. Hartz:** No.

**Dr. Peterson:** How would you differentiate a unicameral cyst from a fibrous cortical defect?

**Dr. Hartz:** The fibrous cortical defect should be specifically confined to the cortex, should be in the

metaphyseal area, and should be asymptomatic.

**Dr. Peterson:** Most of those things are also true of a unicameral cyst. Dr. Duncan, can you think of any things that differentiate a unicameral cyst from a fibrous cortical defect?

**Dr. Douglas M. Duncan:** I think a fibrous cortical defect is usually more eccentrically located and possibly has a little more sclerosis around the edges.

**Dr. Peterson:** Those are the two main features. Sometimes the edges are called "scalloped." One other feature when fracture is present is a fallen fragment sign. What is the fallen fragment sign?

**Dr. Kearney:** It is when a bone fragment falls to the bottom of a simple bone cyst after a fracture.

**Dr. Peterson:** That's correct. The cortex of a cystic lesion will often fragment or shatter when fractured. A little bone fragment may fall to the bottom of the cyst because it is liquid. A fracture in a solid tumor will not produce any fallen fragments. So the absence of the fallen fragment sign doesn't confirm that it is a solid tumor. It still could be cystic with no fragment. But you would not see a fallen fragment sign in a solid tumor. Dr. Hartz, how would you manage this case?

**Dr. Hartz:** I would like to manage this one nonoperatively at first and see if I could line up the



Fig. 5 (Case 2). Closed pathologic fracture of distal right femur.



fractured bones in proximal tibial skeletal traction.

**Dr. Peterson:** A pin was placed in the proximal tibia the night the patient was hospitalized, and 90-90 traction was applied. A short leg cast was applied to balance the traction. Adequate reduction could not be maintained. Various straps and weight alterations were tried in an effort to improve position and alignment, without success. In addition, two closed reductions were done with the aid of general anesthesia and image intensification. The fracture could be reduced anatomically and would immediately slip into valgus. The pull of the gastrocnemii, the large tumor defect, and the smooth, oblique fracture surfaces combined to prevent maintenance of reduction. Is this acceptable (Figures 6 (A) and (B))?

**Dr. Hartz:** No, that is not acceptable. The alignment on the anteroposterior view is fine, but I don't think that on the lateral view is acceptable. The apposition is probably adequate to allow healing, but with that defect there is maybe only 10 to 15% bone contact at this point. If you can't hold the fracture reduced, the leg probably would have to be opened.

**Dr. Peterson:** If it were surgically opened, what kind of apparatus would you consider?

**Dr. Hartz:** I would place a plate in this fracture. You might be able to secure the bones with Steinmann pins and hold them in place with a cast of thin plaster, but you would probably want to curet the defect and insert bone grafts because of the apposition.

**Dr. Peterson:** What about an intramedullary rod?

**Dr. Hartz:** I would prefer not to use a rod. The fracture is quite low, and fragment contact may be difficult to achieve with a rod.

**Dr. Peterson:** Are there any other alternatives to open reduction?

**Dr. Steven F. Hoff:** Angular pins.

**Dr. James H. Dobyns:** The Pease pins.

**Dr. Peterson:** What other name do they go by?

**Dr. Dobyns:** I have not heard of any other name, and I don't think you can even get the pin anymore. The pin lodges against the cortex and comes out on the other side, so that you can put traction on the far side of the pin.

**Dr. Peterson:** "Beaded wires" is the other name (Figures 7(A) and (B)).<sup>5</sup> These wires are no longer made, but Richards now makes a modified skeletal traction pin, which is partially threaded, called the "Kronendonk pin." The principle is to pass the two wires, one from either side, and pull on the lead wire of each pin, squeezing the fractured ends together. In order to hold the reduction, one of the old horseshoe traction bows, which are not commonly used today, is needed. Each

wire fixes into only one side of the traction bow, and a screw device applies tension on the wire. These traction devices were formerly used with thin wires for traction and aren't used much anymore, because we use heavier wires. The disadvantages of these traction bows are that they are not adjustable for size and are heavy. Thus, the fracture was treated closed. The method is applicable to long, oblique tibial fractures. Most of Dr. Pease's cases were this kind. But he used this method in the femur and in the patella, also.

**Dr. Fitzgerald:** This is a good technique to maintain easily obtainable reduction. The traction bow was incorporated into a spica cast. What complications might this method cause?

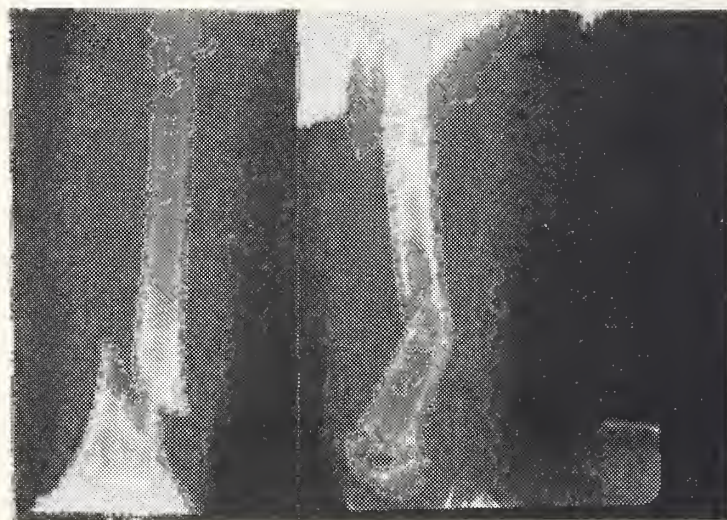


Fig. 6 (Case 2). Five days after injury. Fracture in traction after manipulation under anesthesia. (A-left) Anteroposterior view. (B-right) Lateral view.

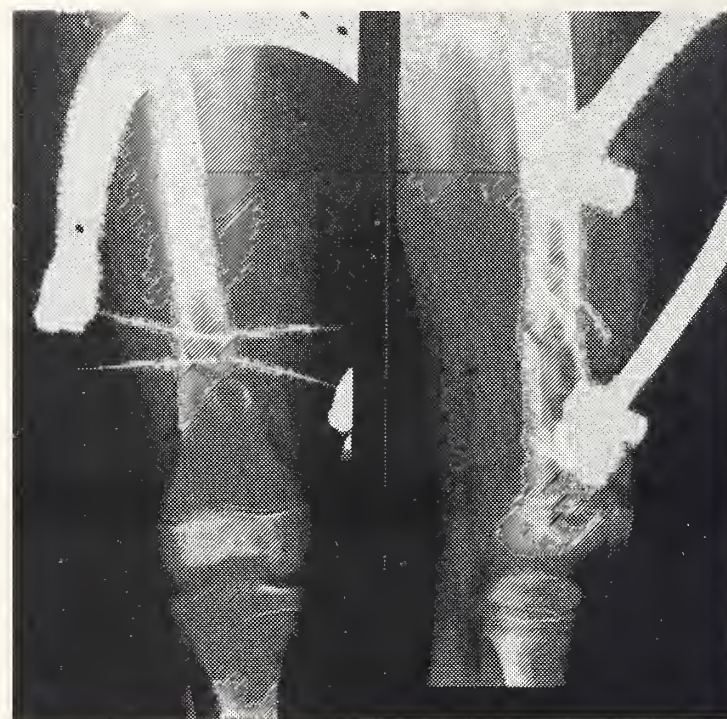


Fig. 7 (Case 2) — Position of fracture fragments after reduction and fixation with beaded wires inserted percutaneously. (A-left) Anteroposterior view. (B-right) Lateral view.



**Dr. Hartz:** The pin might traverse an artery.

**Dr. Fitzgerald:** What about joint complications?

**Dr. Hartz:** Maybe slight stiffness of his knee. Other than that, I wouldn't expect too many.

**Dr. Fitzgerald:** Every femoral shaft fracture in a growing child requires observation for discrepancy in leg length. A year later, the growth plate had grown away from the lesion, which was becoming incorporated into the cortex because of remodeling and tubulation. Three years and eight months after injury, the lesion had nearly disappeared (Figures 8 (A) and (B)).

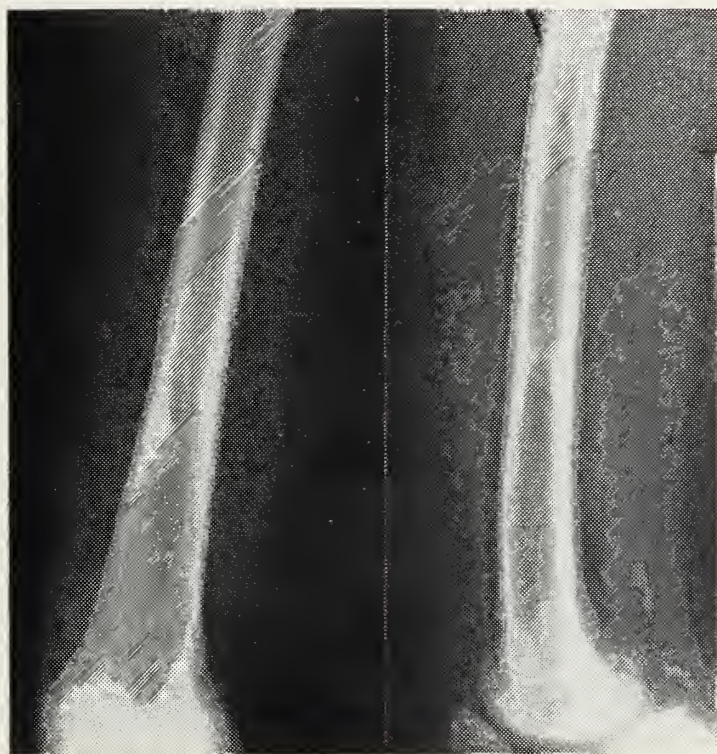


Fig. 8 (Case 2). Fracture well healed three years and 8 months after injury. (A-left) Anteroposterior view (B-right) Lateral view.

**Dr. Peterson:** Scanograms one year after injury showed the involved femur to be 1.6 cm longer. And it remained 1.6 cm longer each year for five years after injury. Thus, no treatment for leg-length discrepancy was needed.

**Dr. Coventry:** Longer or shorter?

**Dr. Peterson:** The involved right femur is longer. It is possible it could have been a little longer before the fracture. All the increased length was noted during the first 6 to 8 months, and length didn't change thereafter.

Dr. Fitzgerald is going to tell us about nonossifying fibromata.

**Dr. Fitzgerald:** Metaphyseal fibrous defects and nonossifying fibromata are indistinguishable microscopically. Clinical differences represent different stages of the same process. A defect in endochondral ossification results in production of fibrous tissue rather than bone in the metaphysis of a long bone.

The first radiologic description of this entity is attributed to Sontag and Pyle.<sup>6</sup> They described findings from a study of serial Xrays in 54 girls and 47 boys. These Xrays were made at birth, three months, and 6 months and every six months thereafter until age 18 years. Lucent lesions developed in the distal part of the femora of 22% of the girls and 53% of the boys. They produced no symptoms and regressed spontaneously. The lesions were first noted in children from two to six years of age, and they lasted an average of two and one-half years.

In 1955, Caffey<sup>7</sup> reported on a similar series. Xray studies were made of both knees and hands of 1,000 children to determine the effect of fluoride. He studied 154 random cases. Forty-two percent of the boys and 31% of the girls had lucent areas in their femora. In boys, the average age at onset was five and one-half years, and lesions lasted an average of four and one-half years. The lesions developed in the girls at an older age, about seven, and lasted two years and one month. However, some lesions persisted for five to eight years.

In 1945, Hatcher<sup>8</sup> reported on 51 lesions in 45 patients. The age at discovery ranged from six to 40 years. All lesions were incidental findings. There were no fractures. Seventeen operations were done for biopsy. Some lesions subsequently ossified, others disappeared because of tubulation, and the rest simply calcified at the rims. In 1956, Maudsley and Stansfeld<sup>9</sup> reviewed 10 cases and diagramed the lesions disappearing by tubulation.

In 1949, Ponseti and Friedman<sup>10</sup> described three lesions that occurred in the same child in the same bone. An Xray made when the child, who had infantile scoliosis, was two years old showed the humerus to be normal. At age four, another Xray revealed the first lesion, which lasted for four years. The second lesion developed at age five and one-half and lasted for seven and one-half years. The third lesion appeared when the patient was nine but it ossified, lasting for only one and one-half years. All the lesions seemed to arise from the same part of the physis.

### Summary

Metaphyseal fibrous defects occurred in a high percentage of normal children. Some defects persisted or enlarged and became nonossifying fibromata. The basic defect seemed to develop from growth cartilage that produced fibrous tissues instead of bone. Boys were affected more often than girls, and their lesions persisted longer. All the lesions occurred in the metaphysis.



Fractures through nonossifying fibromata account for 10% of pathologic fractures of benign tumors in children.<sup>11</sup> The average age at the time of fracture in combined series is 12½ years, whereas in prospective studies, the age at onset of metaphyseal defects is about six years. Comparing data on the incidence and site of fractures allows some clinical conclusions (Table). Whereas almost half the discovered metastatic defects occurred in the femur, only 5% of the fractures occurred there. Only 17% of the metaphyseal defects occurred in the distal tibia, but almost half (48%) of the fractures occurred there. Three percent of the metaphyseal defects occurred in the humerus, yet 14% of the fractures occurred in that bone. Apparently, lesions of the distal tibia and of the humerus are most likely to be associated with fracture.

Several series have reported fractures.<sup>9,12,14,15</sup> Although healing occurs with nonoperative treatment, accelerated filling of the defect does not seem to occur. Curettage and bone graft do not result in complete cure either. In five of 11 fractures treated with curettage and grafting, the lesion persisted or even recurred. Lesions persisted for two and one-half years in four of seven patients treated nonoperatively with casts, but healed in less than two and one-half years in the other three. Review of the literature suggests that humeral and distal tibial lesions are more likely than others to result in fracture. It doesn't tell us what size lesion would be most likely to be associated with fracture, which ones should prompt us to tell children not to go out for

sports, or which ones we should perhaps even treat prophylactically. The literature doesn't assure us that if we did operate on one of these lesions, we could obliterate it with bone grafting and find that a year later the bone was normal.

**Dr. Peterson:** Thank you. We found the literature to be rather scanty, particularly with regard to fractures. There are only 21 cases of fractures through nonossifying fibromata reported in the English literature.<sup>9,12,14,15</sup> The most authoritative paper, reporting 10 cases, is by Drennan and associates.<sup>15</sup> The other cases were isolated reports occurring in articles discussing nonossifying fibromata. Only one of these 21 fractures was opened or compound. The rest were all closed. Thus, the first patient this morning was rather unusual.

**TABLE**  
Distribution of Nonossifying Fibromata

	Lesions*		Fractures†	
	No.	%	No.	%
Femur	37	49	1	5
Tibia				
Proximal	15	20	2	10
Distal	13	17	10	48
Fibula	6	8	3	14
Humerus	2	3	3	14
Radius	1	1	2	10
Ulna	1	1	0	0
Total	75	99	21	101

\*Combined total from three articles<sup>9,12,13</sup> in which attempts were made to determine incidence by anatomic site.

†Combined total from four articles<sup>9,12,14,15</sup> reporting fractures through nonossifying fibromata.

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1980 Minnesota Medical Association 127th Annual Meeting  
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# Clinical Pharmacy

## Glutethimide Overdose

### Clinical and Kinetic Observations of Glutethimide and a Metabolite

JOHN C. ROTSCHAFER, PHARM. D.\*; CHRISTOPHER FOLEY, M.D.\*; and DARWIN ZASKE, PHARM. D.\*

**We describe a patient who had ingested approximately 7.50 GM of glutethimide. Serial concentrations of both glutethimide and a principal metabolite, 4-hydroxy-2-ethyl-2-phenyl-glutarimide (4HG), were measured and the half life for both agents estimated. While the patient did eventually recover, the duration of his intoxication was extended approximately twenty hours beyond the point where the concentration of glutethimide was essentially zero.**

THE ABUSE OF SEDATIVE and hypnotic agents has become a ubiquitous panacea in this country. Frequently, this abuse takes the form of gestural or actual attempts at suicide that require the intervention of a clinician. Glutethimide, a nonbarbiturate hypnotic agent, while not enjoying the popularity once known, is still commercially available and is on occasion associated with intoxication.<sup>1,2,3</sup>

Previously, observers have universally reported a poor correlation between plasma levels of glutethimide and the level of intoxication.<sup>4-9</sup> This has lead investigators to possible explanations including redistribution of the lipid soluble glutethimide,<sup>10</sup> saturation of existing pathways for glutethimide metabolism,<sup>8,11-13</sup> the existence of pharmacologically active metabolites,<sup>8,14</sup> and the possible enterohepatic circulation of glutethimide metabolites.<sup>15</sup>

The existence of an active metabolite has been advanced by Ambre and Fisher.<sup>8,14</sup> This metabolite, 4-hydroxy-2-ethyl-2-phenylglutarimide (4HG), has been identified in human serum,<sup>14</sup> proven to be pharmacologically active,<sup>8</sup> and the decline of this metabolite from serum seems to correlate with improvement in the clinical status of the patient.<sup>8,9</sup>

This communication describes a patient who had ingested a potentially lethal dose of glutethimide. From the measured levels of glutethimide and 4HG, the pharmacokinetic parameters were determined and correlated with the sequelae of glutethimide intoxication.

#### Case Report

A 40-year-old man was presented to the hospital by local police

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Reprint requests to Dr. John C. Rotschafer, St. Paul-Ramsey Medical Center, 640 Jackson Street, St. Paul, Minnesota 55101.

after becoming increasingly lethargic and unarousable. He had been incarcerated the previous afternoon at which time he ingested 7.5 Gm. of glutethimide. The patient was known to have a history of alcoholism and situational depression for which he had been treated at a state hospital one week prior to admission. Initial examination revealed a lethargic male responding to verbal communication and painful stimuli. Blood pressure was 150/100 with a pulse of 96. At this time corneal, gag, and facial reflexes were intact. The rest of the physical exam was normal except for the absence of bowel sound and a positive stool guaiac. Toxicology screen revealed in initial glutethimide level of 24 mcg/ml. Blood chemistry, serum electrolytes, and blood gases were unremarkable. Chest films and skull series were negative. Because the patient was 20 hours post ingestion without significant symptomatology emesis, lavage or administration of activated charcoal were not done.

A second glutethimide level obtained 22 hours post ingestion was 36 mcg/ml. In view of the patient's increasing lethargy, rising glutethimide levels, and concern for the impending rise of 4HG levels, the patient was intubated and placed on IMV at 30% FI O<sub>2</sub>. Initial hydration was begun and a Foley catheter placed. The patient's course tended to be sporadic cycling through periods of lucidity and obtundation. The early hospital course was complicated by overhydration, a chemical ileus, and oliguria. At 50 hours post ingestion, the patient extubated himself and continued to spontaneously resolve.

#### Comment

The clinician should recognize that glutethimide intoxication results from the combined activity of at least two distinct pharmacologic agents, glutethimide and 4HG. The clinical course of the patient may therefore not correlate with serum levels of glutethimide and 4HG. Reaching peak response may take an unexpectantly long period of time due to the pharmacologic synergy between glutethimide and 4HG. The apogee of intoxication should occur somewhere after the peak glutethimide concentration and before the peak 4HG concentration.

The lipid soluble glutethimide is the chemical substrate generating the water soluble metabolite,



4HG. The plasma concentration of 4HG is initially a function of both the drug's formation and elimination. After the substrate has been eliminated from the body thus preventing further 4HG formation, the plasma concentration of 4HG is then solely dependent upon elimination. The 4HG half life as measured in the initial phase was found to be 30.25 hours. The measured half life for glutethimide was 12.90 hours (as fit to a two compartment model by nonlinear regression analysis).

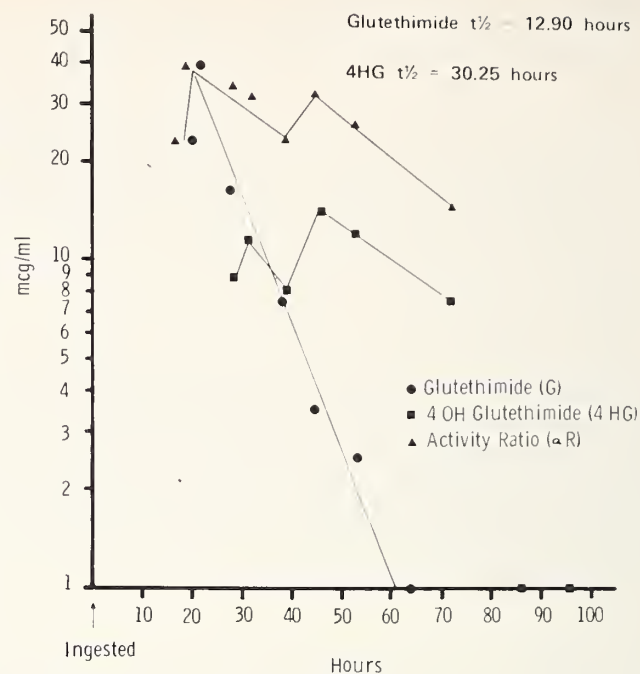
Hansen, Kennedy, et. al. in trying to establish the relative potencies of glutethimide and 4HG encountered a remarkable finding. The metabolite, 4HG, seems to be twice as potent as the parent compound.<sup>8</sup> Fortunately, only about 45% of the parent compound is metabolized to this toxic metabolite.<sup>10</sup> This is especially important when considering that the half life of 4HG is more than twice that of glutethimide. Thus, the duration of intoxication is determined by the rate at which 4HG disappears from the serum. Another consideration is the fact that there are a number of glutethimide metabolites that have not been well studied for pharmacologic activity that may well contribute to the sequelae of glutethimide intoxication.<sup>10,16</sup>

Attempts to incorporate glutethimide and 4HG serum concentration data into a useful clinical prognosticator have been made. This prognosticator has been termed the "activity index".<sup>8</sup> Because 4HG has twice the activity of the parent compound, the "activity index" is the summation of the glutethimide concentration and twice the 4HG concentration. This index value attempts to associate various events of intoxication such as apnea, lack of reflexes, coma and etc.

Attempting to apply activity index values to the sequelae of glutethimide intoxication in this patient met with little success. The failure of the activity index values to correlate with the sequelae of glutethimide intoxication may well be due to the substantial weighting of the activity index value by the 4HG concentration.

As can be seen in the Figure, the serum concentration-time curve for 4HG has an unusual appearance in that 4HG serum concentrations reach two peaks before entering a first order elimination phase. Explanations for this unusual appearance include dilution of the water soluble 4HG by overhydration and possible enterohepatic circulation of the 4HG glucuronide.

The overhydration this patient experienced early in the hospital course may have diluted the 4HG



Figure

concentration and subsequently caused the activity index to be underestimated. The other postulated explanation has been termed "glutethimide rebound" or enterohepatic reabsorption of glutethimide metabolites.<sup>15</sup> The parent compound in the sequence of metabolism initially undergoes hydroxylation and then is conjugated to form the glucuronide. The glucuronide is stored in the biliary tract and ultimately eliminated in the feces. The reabsorption of 4HG from the GI tract may explain the second peak of 4HG seen in this patient.

In therapeutic doses the possibility of enterohepatic circulation of glutethimide metabolites is of little concern. However, in the patient ingesting toxic quantities of glutethimide there are at least two reasons for concern. First, because there is more substrate one would expect more metabolite and because the metabolite is both more toxic and has a longer half life the reabsorption of 4HG from the GI tract will greatly influence depth and duration of glutethimide intoxication. Secondly, high levels of glutethimide may produce a chemical ileus and biliary stasis thus delaying evacuation of the metabolites. The combination of these two problems mean longer storage periods with substantially more metabolite. As the high glutethimide concentrations abate and the ileus and biliary stasis resolve, the metabolite load is released into the GI tract where reabsorption can take place. Effective therapeutic intervention such as the use of oral activated charcoal in conjunction with a saline cathartic may prevent the second phase of the intoxication by binding the metabolite and speeding the evacuation.



### Acknowledgment

We wish to thank Dr. P. Cervoni, USV Pharmaceutical Co. for providing the 4HG needed to produce the standard curve used in our GC assay.

We would also like to acknowledge the assistance of Dr. Ronald Sawchuk in the kinetic analysis of our data.

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### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
3. Has made outstanding contributions to the Medical School, the University, the Alumni, and the community.
4. Has had a relatively long experience in the field of medical science or a related field.

Nominations for the May 1980 awards should be sent immediately to:

Konald A. Prem, M.D., Chairman,  
Harold A. Diehl Award Committee  
Box 395, University of Minnesota Hospitals  
Minneapolis, Minnesota 55455  
(612) 373-7635

Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.

### Have you read NEWSPAGE lately?

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Remember to look for NEWSPAGE in your mail the first week of each month. NEWSPAGE will keep you better informed.



# Minnesota Medical Auxiliary

## Day at the Capitol

Focus on Family Legislation

FEBRUARY 27, 1980

- 9:00 A.M. Coffee/Registration — Room 123, State Capitol, St. Paul  
(Total cost \$6.00, includes coffee, rolls, box lunch  
and materials)
- 9:30 A.M. Orientation — Mrs. Gayle Whitesell, Mrs. Dorothy Diessner
- 9:45 A.M. Welcome — Mrs. William Goodnow, President, MMA Auxiliary
- 10:00 A.M. Optional Events (running simultaneously):  
Art & Architecture Tour of Capitol  
Films on the Legislative Process  
Visits with Legislators  
Audience with Governor
- 11:15 A.M. Speakers:  
Senator Emily Staples  
Representative Robert Reif, M.D.  
Representative Gary Laidig  
George Pettersen, M.D., Commissioner of Health
- 12:15 P.M. Remarks:  
Frank E. Johnson, M.D., President, MMA  
Merle Mark, M.D., Legislative Chairman, MMA  
Mr. James Sova, Director, Dept. of Legislation, MMA
- 1:00 P.M. Box Lunch
- 1:30 P.M. Ross Rubin, J.D., Director, Department of Federal Legislation,  
AMA
- 2:20 P.M. Business Meeting

Yes, this is an ambitious program, but we in Minnesota are leaders in legislation because of our industriousness. We are particularly pleased with the good liaison and excellent communications between the medical association and the auxiliary. As partners, we can continue to promote good health care legislation in Minnesota. Because personal contact is the key to favorable legislation, ample opportunity will be given to auxiliaries to personally invite their legislators to join us. The speakers will be of interest to all. Our legislative goal this year is to become as informed as we can be on health care legislation affecting the family. Here's a beautiful chance. So — barring a blizzard, we expect to see you all in St. Paul on February 27.

Gayle Whitesell and Dorothy Diessner  
State Legislative Co-Chairs



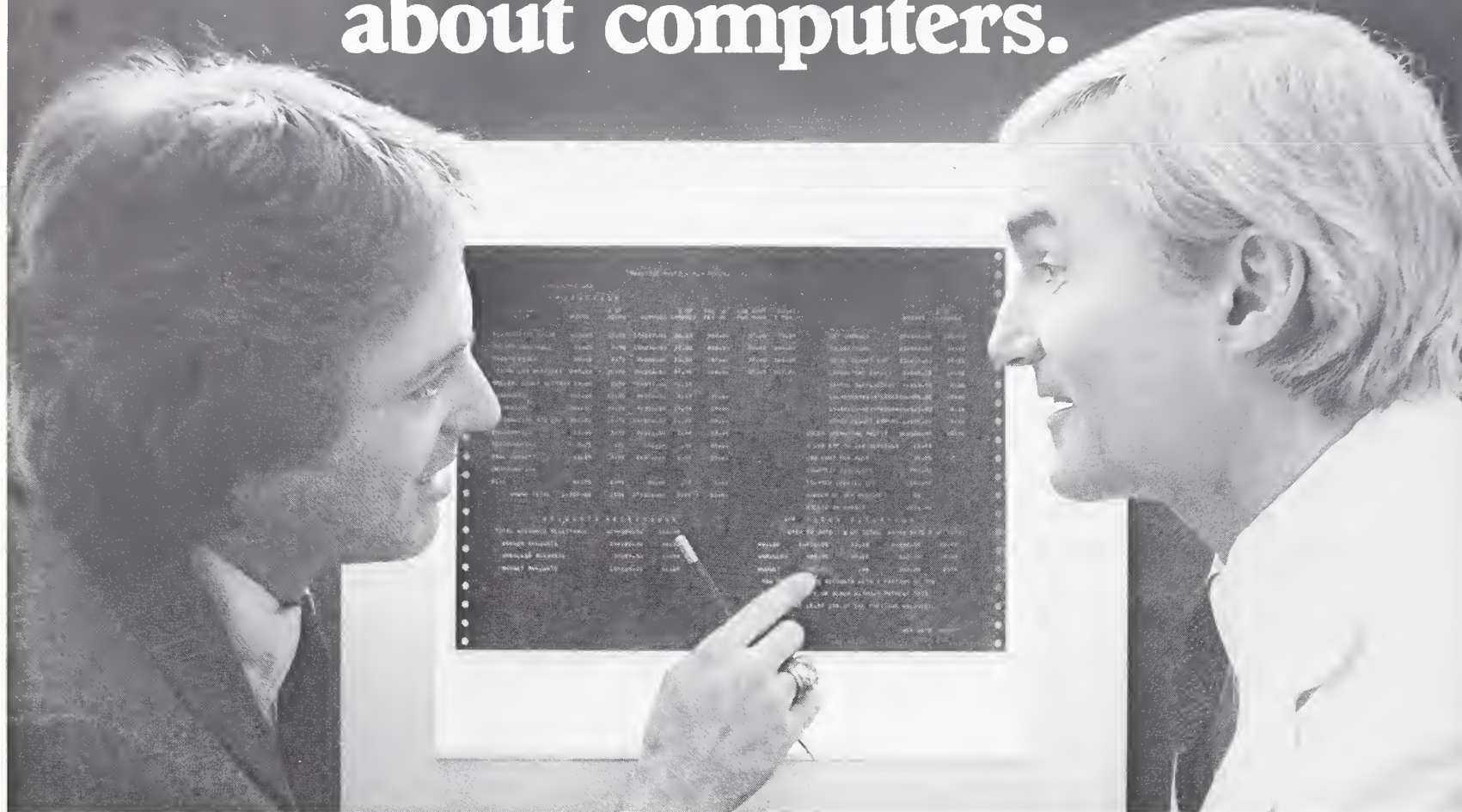
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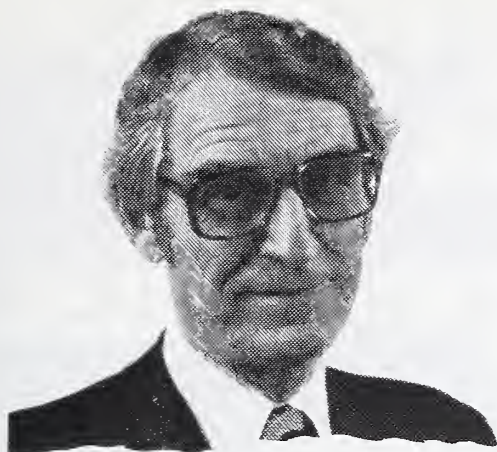
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## President's Letter

The matter of professional liability insurance and the philosophy of underwriting, claims management, and premium structure continues to occupy the attention and be a concern of your Association. With the aid of our consultant, Johnson & Higgins Company, we have, over the past three years, developed an increased understanding of how the St. Paul Companies manage this portion of their business. Nevertheless, certain questions remain incompletely answered and perhaps it is unrealistic to expect more from a private business corporation.

While negotiations continue on your behalf, with the St. Paul Companies, we have, at the direction of the House of Delegates, at our annual meeting in 1979, explored the option of forming an insurance company under the control of the MMA. To this end, a careful study was conducted by a highly respected actuarial consultant, Mr. David Bickerstaff of Milliman & Robertson, Inc. The data and its analysis resulting from that study were then interpreted by Mr. John Dorsett of American Health Systems, Inc. This firm has an excellent reputation and a long experience in consulting with medical associations on professional liability programs and in establishing physician owned companies. Additional assurance is gained from the fact that they served us well in developing the Foundation for Health Care Evaluation and the Physician's Health Plan in the Hennepin County metropolitan area. Both of these organizations are now soundly established.

A steering committee received Mr. Dorsett's final report on January 15, and on January 19, your Board of Trustees acted favorably on its recommendation that we proceed to form a physician owned insurance company "on paper." It authorized expenditure of up to \$50,000 to accomplish this. That sum will be repaid to the Association with interest if and when the company is successfully established.

Our approach in capsule form is to plan a physician owned company to be domiciled in Minnesota, subject to its laws and under the careful scrutiny of the Commissioner of Insurance, both of which are designed to protect policy holders. The organizational

design and necessary legal work for such a company will be accomplished so that the proposal may come before the House of Delegates. Assuming approval of the House of Delegates, we would be prepared to immediately institute a drive for capital contributions from our members. Final figures have not been developed at this time, but it is estimated that the basic contribution for a class 1 physician would be about \$1,000. This amount would be scaled upward according to a physician's risk category. At this time it appears that policies offering coverage similar to that which we now carry could be issued to members of the captive company at a saving of 25-30 per cent. This means, of course, that our capital investment would be recouped within a few years. In addition it is planned that the capital investment would be returned at the time one leaves practice.

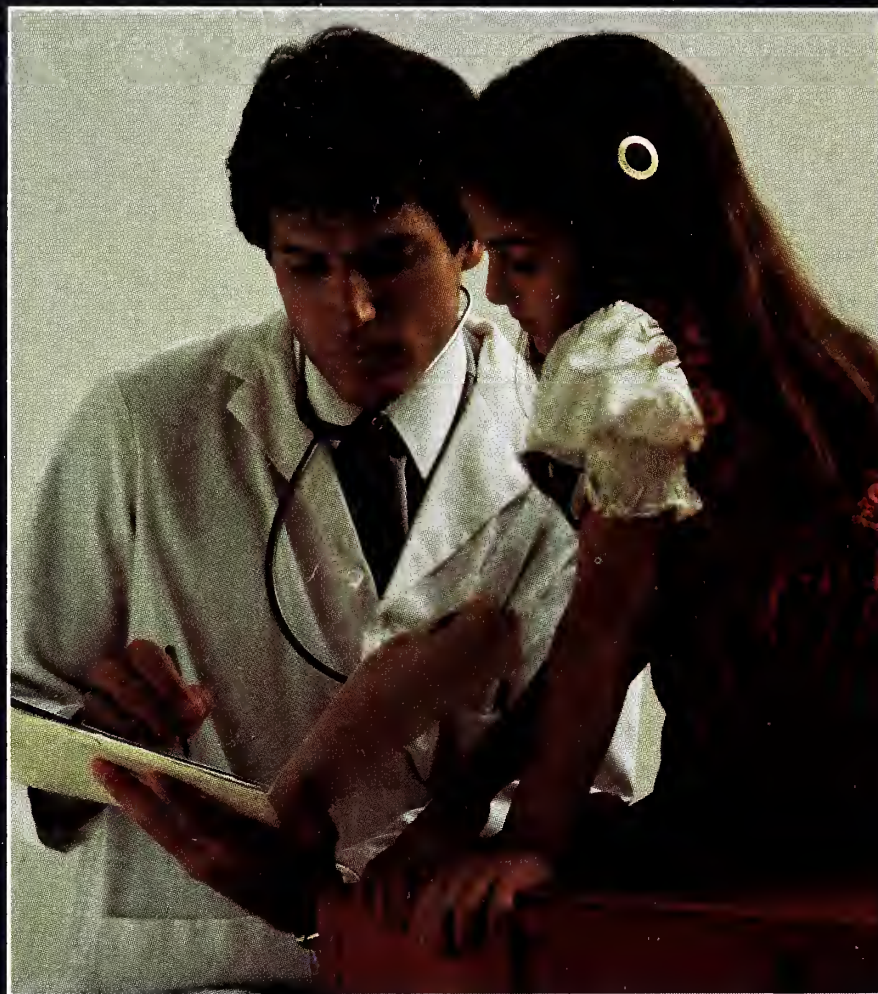
The advantages of a physician owned insurance company as I see them are: (1) The books would be completely open to the membership so that there need be no question how the premium dollar is spent. All investment income and savings in operation will accrue to the benefit of the participating physicians. (2) Having our own company might make us more aware of the numerous facets of professional liability, i.e., I could envision a more wide-spread interest in underwriting and risk management than now exists. (3) A successful flourishing physician owned company which restricted coverage to those physicians who are members of the Association might prove to be of significant help in the important area of membership recruitment. (4) Sharing of capabilities such as computer data processing with MMA could have a definite dues sparing effect.

It is my hope that with your help, the MMA professional liability insurance company will be solidly in place and operational by July 1, 1980.

Frank E. Johnson, M.D.  
President  
Minnesota Medical Association



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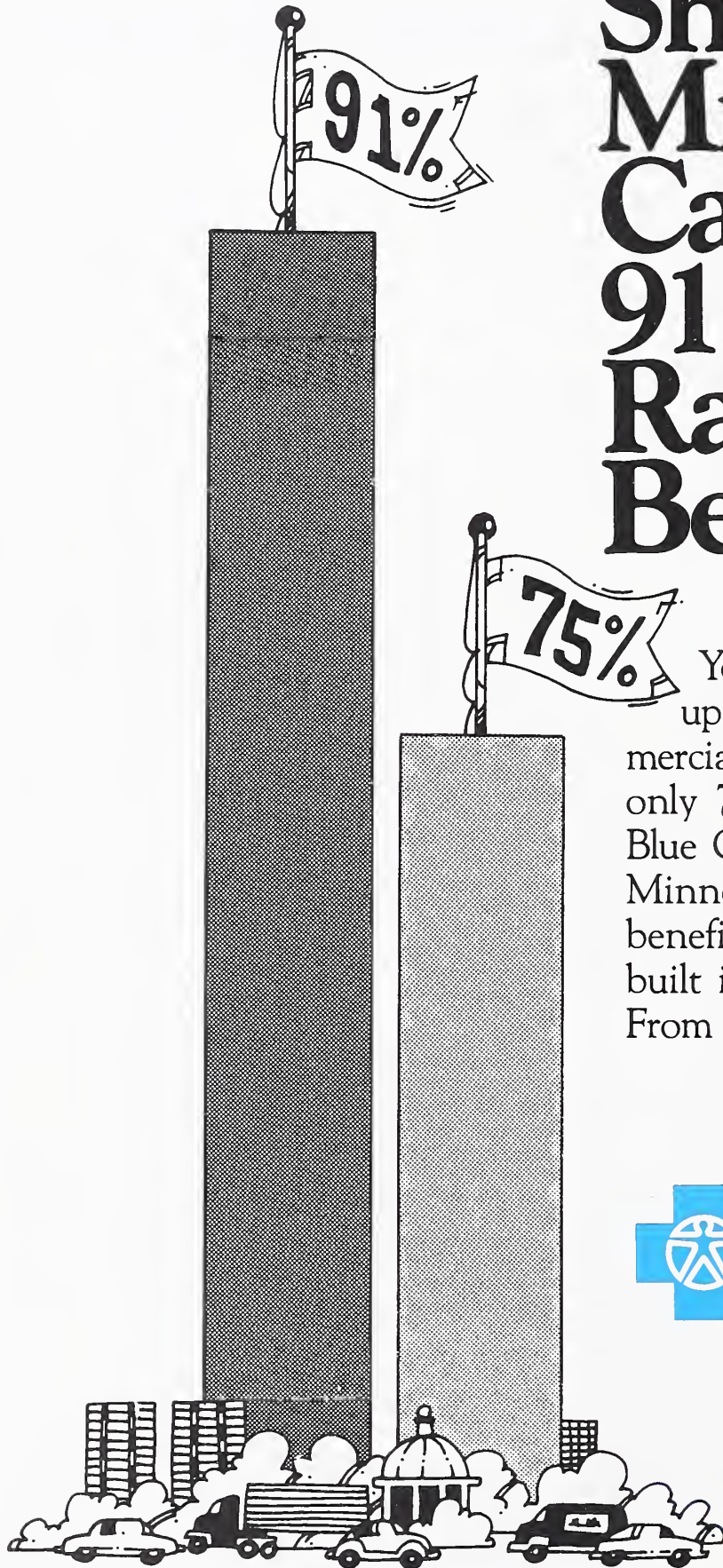


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MARCH, 1980



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# Breast Cancer

## Improving Long-Term Survival

VICTOR A. GILBERTSEN, M.D.\* and JANET M. NELMS, M.P.H.†

**A thirty year study of cancer of the breast casts serious doubt on the value of mammography in the detection of cancer for any but highly selected cases.**

CANCER OF THE breast continues to be the most common fatal neoplasm which occurs in women in this country. Follow-up studies indicate that while most women who develop breast cancer are alive at five years, later recurrences are not uncommon and more than half eventually die of the disease.

The development of refinements of X-ray breast examination techniques suggested the possibility of facilitation of detection of earlier cancers. Publication of survival results of several studies utilizing such techniques led to enthusiasm for use of mammography in screening of asymptomatic women for breast cancers.<sup>1</sup>

The feasibility of widespread employment of mammography as a means of reducing mortality from breast cancer apparently was presumed.<sup>2</sup> Several dozen breast cancer "demonstration" centers were established for periodic examinations of substantial numbers of women throughout the country. The rationale for establishment of the demonstration centers, for the most part, appears to have been based on the improved survival observed for women with cancers found on mammography compared with survival of cancer patients who did not undergo periodic examinations.

The present study reports survival data regarding women enrolled in a program of periodic physician examinations/self examination. Follow-up data indicate that substantial improvement in survival occurred in association with periodic physician examinations even without the addition of mammography to the examination protocol.

### The Study

The Cancer Detection Center was established at the

\*Associate Professor and Director, Cancer Detection Center, University of Minnesota Medical School, Minneapolis.

†Associate Scientist, University of Minnesota Medical School, Minneapolis.

This study was supported in part by the Fraternal Order of Eagles Fund for Research in Cancer.

University of Minnesota in 1948 to aid in evaluation of the merit of various procedures in the earlier detection of cancer. Details of the operation of the study have been previously reported.<sup>3</sup>

From 1948 through 1971 — the period for which at least a five-year follow-up is available — 8649 women participated in the study. Each was 45+ years of age upon entrance into the program and agreed to return for annual examinations for as long as such would be feasible. The 8649 women underwent a total of 49,000 annual examinations or an average of 5.6 per participant.

Periodic evaluations included breast examinations by methods of physical diagnosis. Participants were instructed regarding breast self-examination and were advised to seek prompt medical attention in the event an abnormality should be found.

Cancers detected on annual examinations at the Center numbered 65. 63 of the 65 patients were five-year survivors for an absolute 5 year survival rate of 97%.

Fifteen year follow-up is available for the 35 patients with breast cancers detected 1948 through 1961. 25 of the 35 (71%) were 15 year survivors. The relative 15 year survival rate was 100%.

During between-examination intervals 53 cancers of the breast were found. 39 of the 53 (74%) patients were five-year survivors. The relative five-year rate was 80%. 21 of these patients could be followed 15 years or longer; 12 of the 21 (57%) lived at least 15 years; and the relative 15 year survival rate was 78%.

Overall, 118 cancers of the breast developed in Cancer Detection Center participants — 1948 through 1971. 102 of the 118 patients (86%) survived at least five years; the relative five year rate was 95%. 56 patients could be followed for 15 years or longer; 31 of the 56 (66%) were 15 year survivors; and the 15 year relative survival rate was 96%.



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Each gram of Anusol-HC Cream contains hydrocortisone acetate, 5.0 mg; bismuth subgallate, 22.5 mg; bismuth resorcin compound, 17.5 mg; benzyl benzoate, 12.0 mg; Peruvian balsam, 18.0 mg; zinc oxide, 110.0 mg; also contains the following inactive ingredients: propylene glycol, propylparaben, methylparaben, polysorbate 60 and sorbitan monostearate in a water-miscible base of mineral oil, glyceryl stearate and water.

**Indications:** Anusol-HC Suppositories and Anusol-HC Cream are adjunctive therapy for the symptomatic relief of pain and discomfort in: external and internal hemorrhoids, proctitis, papillitis, cryptitis, anal fissures, incomplete fistulas and relief of local pain and discomfort following anorectal surgery.

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**Contraindications:** Anusol-HC Suppositories and Anusol-HC Cream are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

**Warnings:** The safe use of topical steroids during pregnancy has not been fully established. Therefore, during pregnancy, they should not be used unnecessarily on extensive areas, in large amounts or for prolonged periods of time.

**Precautions:** Symptomatic relief should not delay definitive diagnoses or treatment.

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In the presence of an infection the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

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Anusol-HC is not for ophthalmic use.

**Dosage and Administration:** Anusol-HC Suppositories — Adults: Remove foil wrapper and insert suppository into the anus. Insert one suppository in the morning and one at

bedtime for 3 to 6 days or until inflammation subsides. Then maintain patient comfort with regular Anusol Suppositories.

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### Discussion

Most of the breast cancers (55%) which developed in participants in the study were detected on annual physical examinations at the Center. All but two of the 65 patients with cancers detected at the Center lived at least five years; one patient died in less than a month of metastatic cancer and another died of an unrelated cause.

The five year relative survival rate of 100% for those with cancer detected at the Center compares favorably with the 60% rate reported elsewhere.<sup>4</sup> The relative rate remained 100% at 15 years, i.e., for at least 15 years patients with breast cancers which were detected at the Center survived at a rate no less favorable than that of women in the general population without breast cancer. Usually reported survival of breast cancer patients continues to deviate from "normal" and at 15 years has been reported as 43%.<sup>4</sup>

Most of the cancers found during between-examination intervals were detected by breast self-examination. Long-term survival of these patients, although less favorable than that for those with cancers found at the Center, was substantially improved from that usually noted for patients with this disease, i.e., 78% relative survival at 15 years.<sup>4</sup>

The overall survival for all participants who developed breast cancers was at five years 95% of that "normally" anticipated for women without breast

cancer and continued to be equally as favorable for at least the 15 year follow-up of the study.

Cancers of the breast developed among Cancer Detection Center study participants at a rate of 2.4 per thousand patient years (118 per 49000 patient years). This rate is in correspondence with that usually observed for comparable women in the population of Minnesota. This may be contrasted with the rates of detection reported from several studies utilizing mammography, rates 5+ times the anticipated incidence of the disease.

### Conclusions

Follow-up studies demonstrate that the rate of survival of Cancer Detection Center participants who developed breast cancers was at five years 95% of that anticipated for normal women without breast cancer and remained equally as favorable for at least the 15 year period of follow-up study.

Improvements in long-term survival associated with periodic screening for breast cancer would appear to be associated for the most part with physician examination/self-examination aspects of such programs. The results of the present study suggest that the potential for further enhancement of survival by addition of X-ray examination procedures to such periodic screening endeavors is likely to be severely limited.

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# Falciparum Malaria in Minnesota

PAUL KUBIC, M.D.\*; CAROLYN LEVITT, M.D.†; and PETER COCCIA, M.D.‡

**Malaria must be considered in any febrile patient recently returned from the tropics. Five recent St. Paul cases remind us that early diagnosis and prompt therapy is necessary in thwarting this potentially fatal disease.**

**M**ALARIA IS ONE of the most common infectious diseases of man, causing much morbidity and mortality mainly in the tropical areas of the world.<sup>1</sup> In the United States, malaria is a non-epidemic disease with protean manifestations. Therefore, fever in an individual who has either traveled or lived in a country where malaria is endemic should alert the physician to the possibility of this disease.

Five previously undiagnosed cases of malaria in two families have recently been treated at St. Paul Children's Hospital. We would like to share our experience by reviewing the presentation, diagnosis and management of these children. It is hoped that others will also be aware that in an age of international travel, tropical diseases do occur in temperate climates and that potentially serious delays in diagnosis and treatment may be avoided.

## Case Reports

### Case 1.

An 11 year old white male had been living in Tanzania, Africa for over one year where his father was employed by the government. He was in good health until beginning his return to the United States via Greece and Europe. He had taken chloroquine prophylactically during his stay in Africa and for two weeks after his departure. Approximately four weeks prior to his admission he began to complain of myalgias, leg weakness, lethargy, anorexia, nausea and vomiting. Intermittent fevers of undefined periodicity occurred. Two weeks prior to admission, recurrent severe headaches were noted with fevers spiking to 40°C. He was seen by several physicians in England and the United States who prescribed symptomatic therapy and fever control for a non-specific gastroenteritis. The patient was finally seen by a family physician in rural Minnesota who noted an anemia and reticulocytosis, and suspecting a tropical disease, referred the patient to St. Paul Children's Hospital for evaluation.

On admission his temperature was 38.7°C., pulse 100, blood pressure 94/48, weight 30 kg. (approximately 2 kg. below his weight in Africa). The physical examination revealed a pale, lethargic

young man. A Grade II/VI systolic murmur was noted. His spleen tip was palpated 4-5 cm. below the left costal margin and was mildly tender. A tender liver was palpable 4 cm. below the right costal margin with a total span of 14 cm. The remainder of the physical exam was normal and no neurologic abnormalities were noted.

Laboratory studies showed a hemoglobin of 7.3 gm./dl, a leukocytic count of 3000/cu. mm. with 32% neutrophils, 64% lymphocytes, 4% monocytes, a platelet count of 176,000 cu mm and 6.9% reticulocytes. Total bilirubin, direct Coombs and G6PD screen, coagulation studies, urea nitrogen and urinalysis were all normal. Serum sodium was 130 meq/l. A thin smear of the peripheral blood revealed abundant crescent or banana-shaped gametocytes, diagnostic of *Plasmodium falciparum*.

The patient was started on oral chloroquine phosphate, 10 mg. base/kg. initially and 5 mg./kg at six, 24 and 48 hours after the first dose. Defervescence occurred within twelve hours and he was ambulatory and on a full oral diet after 24 hours. Two days later the hemoglobin was 7.8 gm/dl, platelets of 103,000/cu mm. and normal serum sodium. He was discharged on Folic acid and blood counts and smears were followed twice weekly by his family physician. Ten days after discharge his spleen tip was still palpable but the physical and neurological examination were otherwise normal. His hemoglobin and hematocrit were 9.7 gm/dl and 29% respectively, platelets were 238,000 cu mm and reticulocytes 10%.

### Case 2.

Our next patient is the 10-year-old brother of the preceding patient. He was also seen by multiple physicians who diagnosed gastroenteritis. He remembered having cold sores early in the illness.

On admission he was febrile, pale and ill appearing with tender splenomegaly. He was oriented and fairly alert. His hemoglobin was 8.1 gm/dl., WBC 31,000/cu. mm. with 41% neutrophils, 57% lymphocytes and 2% monocytes. Platelets were 211,000/cu mm. and reticulocytes 9.1%. His erythrocyte sedimentation rate was 65 mm/hour. Total bilirubin was 1.5 mg./dl, sodium 128 meq/l. A thin and thick peripheral smear demonstrated numerous *Plasmodium falciparum* gametocytes. He was treated with chloroquine as in Case One. Defervescence and striking improvement occurred within a day. He was discharged on day 3 with a platelet count of 49,000/cu mm., sodium of 135 meq/l, and normal urinalysis. His platelet count began to rise within two days. On return to our clinic in ten days, he had a normal physical and neurologic examination, his hemoglobin was 10.3 gm/dl, WBC 4400/cu mm with 32% neutrophils, 66% lymphocytes, reticulocytes 11.9%, 122,000 cu mm platelets and occasional gametocytes on the thin smear.

The parents and other siblings never experienced the signs or symptoms of malarial infection. Hematological examination

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including thin and thick blood smears were normal in the remaining family members.

#### Cases 3, 4, & 5.<sup>2</sup>

These patients were all members of the same black African family. Case 3 was a 7 month old female, Case 4 a 2-year-old male, and Case 5 a 4-year-old male, who had recently arrived from Zaire, Africa. The father was a college student in St. Paul.

All were seen in the St. Paul Children's Hospital Emergency Room. Case 4 was in status asthmaticus and was admitted for treatment. The other two children had identical complaints of anorexia, mild lethargy and fever of one week's duration. A worm had been found in the stool of Case 3 earlier in the week.

Case 3 was pale, mildly febrile and had a 5 cm. palpable spleen. Physical examination of Case 4 was compatible with acute asthma, but otherwise negative. Case 5 was normal on examination.

Stool specimens and complete blood counts were obtained on all the children. Case 3 had a hemoglobin of 6.7 gm/dl, a WBC of 9900/cu mm. with 20% neutrophils and 72% lymphocytes. Case 4 had a normal blood count. Case 5 had a hemoglobin of 9.0 gm/dl., a WBC of 4900/cu mm. with 22% neutrophils and 72% lymphocytes. The family was asked to return to the clinic for evaluation of their anemia.

Upon re-evaluation in two days, Case 3 had a hemoglobin of 7.9 gm/dl, with a reticulocyte count of 17.4%. The peripheral smear showed gametocytes of *Plasmodium falciparum*. The patient was then admitted to the hospital where treatment with chloroquine was initiated. No other laboratory abnormalities and no evidence of organ system complications of malaria were noted. She remained stable during her stay and was discharged after 3 days. Her hemoglobin was 9.3 gm/dl. and reticulocytes 22.4%. Blood counts and smears were re-evaluated on subsequent clinic visits and no evidence of malarial parasites were again found. Ova of *Ascaris* and *Trichuris* were present in the stool and appropriate therapy was initiated.

The smear from Case 5 was later re-examined and occasional malarial parasites were seen. In clinic he was healthy appearing and the examination was unrevealing. He was treated with chloroquine as an outpatient. Ova of *Ascaris* and *Trichuris* were noted and treatment was given. Clinic followup revealed no recurrence of parasites. Case 4 was also seen at this clinic visit and physical examination was normal. A peripheral smear was obtained and after careful review showed malarial parasites. He also was treated as an outpatient. Later examination showed no evidence of malaria. Examination of the parents' smears showed no evidence of malarial infection.

#### Discussion

Several aspects of the above cases deserve comment. Most patients with malaria who are seen in the United States have been infected while visiting or living in a tropical country. In Tanzania and Zaire, epidemiologically, *P. falciparum* is the most common malaria parasite. Several physicians in the United States and Europe misdiagnosed Cases 1 and 2 and apparently did no laboratory studies to evaluate recurrent fevers in patients from a tropical country. *Falciparum* malaria is the most readily diagnosed type of malaria on the peripheral smear as both reticulocytes and older erythrocytes are parasitized. Therefore, a higher percentage of erythrocyte infection is microscopically visible.<sup>3</sup> The diagnosis in Cases 1 and 2 was

made by examination of routine peripheral blood smears. Identification of gametocytes required careful examination of thin and thick smears in the other three cases. If malaria is suspected, blood smear examination should be done every six to twelve hours in an attempt to confirm the diagnosis.

No sign or symptom is pathognomonic of malaria. Most patients have intermittent episodes of fever, chills, headache, and myalgia, all of which are especially prevalent in *falciparum* malaria. Muscle weakness may persist for weeks after therapy. Nausea, vomiting and diarrhea occur less frequently. Splenomegaly is found in about 50% of patients, hepatomegaly less commonly. Labial herpes is often present (as in Case 2).<sup>4</sup>

Anemia is usually mild and due to both increased erythrocyte destruction and decreased erythrocyte production, although a reticulocytosis is often eventually seen. Folic acid deficiency sometimes complicates the anemia. Leukopenia is more common than leukocytosis. Thrombocytopenia (mildly present in Case 2) is often seen with *falciparum* malaria but rarely leads to clinical hemorrhage. Disseminated intravascular coagulation is one of the dreaded complications of *falciparum* malaria and coagulation should be monitored in the ill patient. Coagulation abnormalities leading to focal tissue ischemia may be fundamental to the pathologic process in most complications of *falciparum* malaria.<sup>5</sup>

Mild to moderate hyponatremia, as seen in Cases 1 and 2, is frequently noted with *falciparum* malaria. Sodium depletion secondary to vomiting, diarrhea and mild inappropriate antidiuretic hormone secretion have been proposed as causes. Intravenous hydration should be used with caution to prevent seizures.<sup>6</sup>

Delay in the diagnosis and treatment of *falciparum* malaria may be disastrous and the treacherous nature of *falciparum* malaria cannot be overemphasized. Headache, drowsiness, and prostration may precede alarmingly rapid neurologic deterioration. Cerebral malaria may produce coma and acute circulatory collapse as terminal events. Signs and symptoms of neurologic involvement must be carefully monitored.

Blackwater fever is an ill-defined entity associated with *falciparum* malaria that includes hemolysis, hemoglobinuria, profound anemia and acute renal failure. Renal failure may also accompany malaria without hemolysis and hemoglobinuria, possibly secondary to local hypoxia caused by sludging of parasitized erythrocytes.<sup>7</sup>

Once the diagnosis of *falciparum* malaria is confirmed, therapy should commence without delay.



If neurologic involvement seems likely, the patient is best managed in an intensive care unit with accessible laboratory facilities.

Because fewer than 20% of the erythrocytes on the smear were parasitized and the clinical picture of our patients did not suggest impending neurologic, gastrointestinal, or renal complications, we elected to treat with standard doses of chloroquine phosphate.<sup>8</sup> Recently resistant *falciparum* strains have been reported from Tanzania.<sup>9</sup> Therefore, alternate therapy, as recommended by Trenholme and Carson, must be considered in the patient who does not improve or deteriorates on chloroquine treatment.<sup>10</sup> In the presence of greater than 20% erythrocyte parasitization, impending systemic complications, a platelet count less than 20,000 cu mm or uremia, the treatment of choice would be intravenous quinine hydrochloride. Scrupulous attention to supportive care would include appropriate fluid and electrolyte therapy. Dialysis could be lifesaving if the patient were in acute renal failure.

Prophylaxis of *falciparum* malaria is all-important.

Cases 1 and 2, their parents, and their siblings were treated for only two weeks after their departure from Tanzania. Retrospectively the malarial infections in these three patients probably occurred when the family left their home in a large city in Zaire, an area relatively free of malaria. They traveled to a smaller town on the west coast of Africa in a mosquito infested area. It was here prior to their departure for the United States that the parasite was probably acquired. The most recent recommendation strongly suggests one to two months of prophylaxis after departure from the malarial zone.<sup>11</sup>

In summary, fever in a patient returning from a tropical zone requires consideration of malaria. Diagnosis should be aggressively pursued and therapy promptly initiated. Appropriate prophylaxis should be given to all who travel to or return from endemic malarial areas.

#### Acknowledgment

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# Metastatic Cerebral Choriocarcinoma during Pregnancy

STEPHEN A. MC CUE, M.D., FACOG\* and JACK B. GREENE, M.D.†

This is a case presentation of a 20-year-old primigravida presenting with symptoms of eclampsia who developed a "stroke" pattern shortly after delivery of a normal premature infant by C-section. Rapid diagnosis and surgical evacuation of a hematoma due to metastatic cerebral choriocarcinoma then allowed accepted chemotherapeutic and radiation therapy to be instituted. This paper emphasizes the need to consider metastatic choriocarcinoma in any gravid female who presents with unusual neurologic signs because of the life threatening nature of this potentially curable disease.

**M**ETASTATIC CHORIOCARCINOMA is a rare tumor which presents in a variety of ways depending upon the site of the metastatic lesion. It has only been in the last few years that a reasonable hope of complete cure of this lesion has been made possible.<sup>1</sup> Progress has been rapid and metastatic choriocarcinoma now represents one of the few malignant tumors considered curable after systemic spread has occurred.<sup>2</sup> The problem of obtaining a cure depends upon recognition of this malady in its unusual presentations and the prompt attention to life threatening symptomatology. In particular, metastatic lesions to the brain, lungs and gastrointestinal tract can be fatal before choriocarcinoma is even suspected.<sup>3</sup>

The following case is being presented as an example of a widely disseminated tumor which was unsuspected until the development of a life threatening situation. Furthermore, it represents a choriocarcinoma coexistent with a normal first pregnancy which produced a viable infant and dramatic response to treatment with probable cure of the mother.

## Case Report

A 20-year-old primigravida, EDC is 11-22-76, LNMP 2-15-76, was admitted on September 24, 1976 at 32 weeks of gestation after an episode of vaginal bleeding. During the two weeks prior to admission, the patient admitted to a brownish vaginal discharge and headaches of increasing severity. Immediately on admission, the

patient experienced a generalized seizure and was given 5 grams of intravenous magnesium sulfate. The seizure lasted approximately 5 minutes. On physical examination the patient had a normal fundoscopic examination, her abdomen was consistent with a 30 — 32 week pregnancy, she had +1 pitting edema of the ankles. There were no focal neurologic findings. Vaginal exam was made difficult by a 3 x 4 cm. egg shaped mass along the posterior proximal urethra and the cervix was found to be closed. Fetal heart tones were 160, with fetal weight estimated at 4 pounds. The patient's vital signs were as follows; blood pressure 112/68, pulse 100, respirations 36, and temperature was normal. Laboratory studies demonstrated: 2+ proteinuria, hemoglobin 11.5, WBC 17,300 with normal differential and a potassium of 3.6.

About 20 minutes following the generalized seizure, the patient's blood pressure began to fall and reached 70/50 while the heart rate increased to 120. It was felt that the patient was eclamptic and that vaginal bleeding was secondary to placental abruption with hypotension due to blood loss. An emergency C-section was performed, and a viable four-pound male infant with Apgars of seven

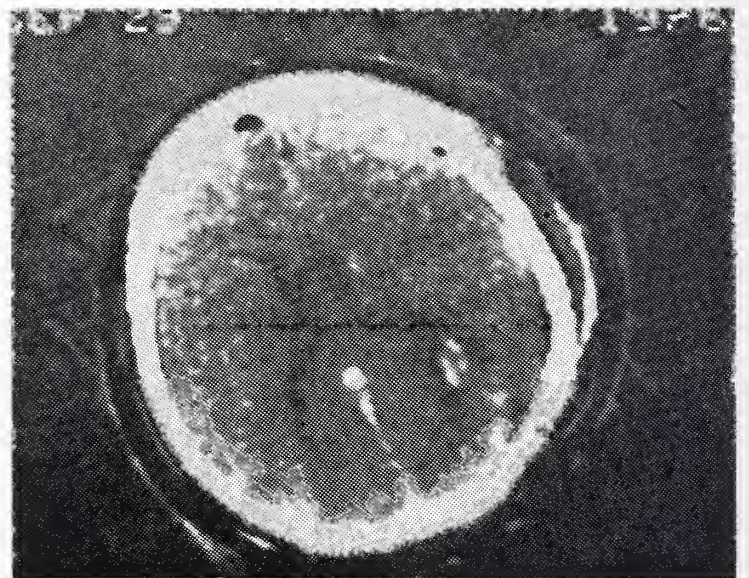


Fig. 1 — EMI scan showing an area of increased density which could represent hematoma or a second tumor mass.

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and eight was delivered. The prior vaginal bleeding was found to be related to a partial placenta previa.

In the recovery room, the patient suddenly developed anisocoria and a left hemiplegia. A right carotid angiogram disclosed a large right fronto-parietal mass and an emergency craniotomy was performed within two hours of the original surgery. At craniotomy a 4 x 4 x 3 cm. mass was identified which appeared to be partially encapsulated and was largely made up of blood clots interspersed with small pieces of light colored tissue. Following surgery the patient's neurologic deficits improved.

Subsequent microscopic examination of the tissue from the mass disclosed a metastatic choriocarcinoma. Gross and microscopic



Fig. 2 — AP chest tomogram showing a right pulmonary mass.

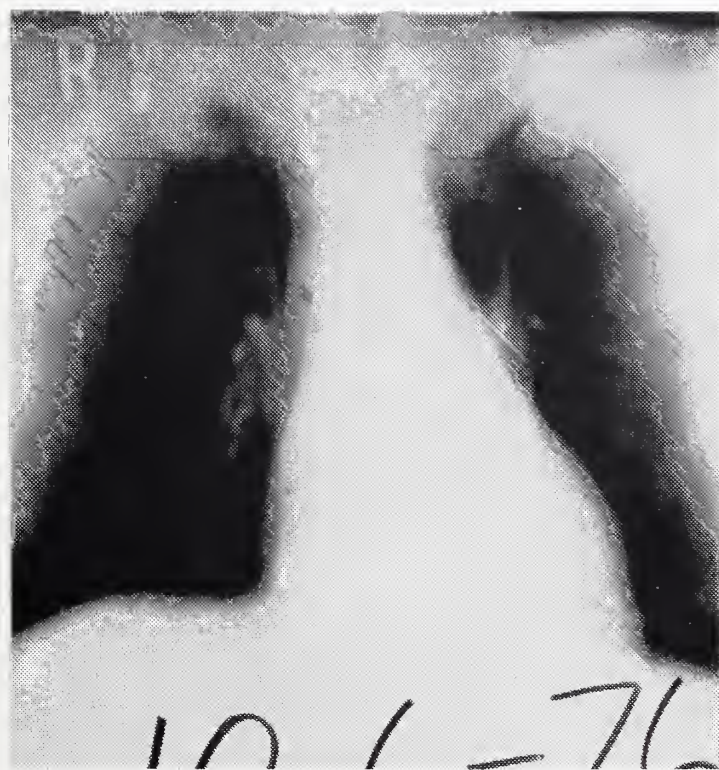


Fig. 3 — Chest tomogram with several apparent lesions.

pathologic evaluation of the placenta failed to demonstrate a primary lesion. A follow up EMI scan done on September 29, 1976 revealed a 1 x 2 cm. area of increased density in the right parietal lobe which could represent further hematoma or another tumor mass (Figure 1). A chest x-ray on 9/25/76 was read as normal, but a subsequent study demonstrated multiple metastatic lesions which were confirmed by tomography (Figure 2). An HCG done on September 28, 1976 showed a level of 390,000 I/U/L.

Chemotherapy was begun on 10-3-76 with Cytosin, Methotrexate, Actinomycin-D, and Vincristine. The protocol used was as follows:

Actinomycin-D, 0.5 mg., Methotrexate, 15 mg and Cytosin, 200 mg. each administered intravenously for five consecutive days with I.V. Vincristine, 1.5 mg. added on the fifth day of the treatment. A second course of treatment followed after a three week interval with a total of four more series. The last two treatments were decreased to four and three days respectively due to nausea. The patient also received cobalt radiation with a total of 4300 rads directed to the whole brain over five weeks. Progress of the treatment was monitored by serial HCGs<sup>4</sup>, which rapidly declined to normal levels within ten weeks. Two subsequent titers were obtained and have been normal. Both the pulmonary and vaginal lesions cleared within one month following initiation of therapy. At the time of this writing, the patient is three years post delivery and doing well.

### Discussion

There are several unique and important aspects to this case. One distinguishing feature is that this tumor appeared in a primipara. Gurwitt in his literature review found no other cases other than his own where intracranial hemorrhage due to cerebral metastasis was the first sign of metastatic choriocarcinoma. His case, however, was in a female with three prior spontaneous abortions. While trophoblastic disease in pregnancy is associated with an increased incidence of pre-eclampsia,<sup>10</sup> the seizures in our case in retrospect were secondary to the cerebral mass lesion. It should also be emphasized that when a gravid patient presents with seizure or other neurologic symptoms, cerebral lesions should be considered in the differential diagnosis.<sup>5,6,7,11,12</sup> In this case the combination of suspected eclampsia and abruption in fact represented cerebral metastatic disease and partial placenta previa. One additional point to be emphasized is that metastatic cerebral choriocarcinoma is a very responsive tumor providing that the patient survives the initial presenting event.<sup>6,13-15</sup> The generally poor prognosis determined for patients with HCG titers over 100,000 and cerebral lesions may occur because a large number of the patients do not survive the initial crisis, and, therefore, do not receive therapy.<sup>13,16</sup>

### Conclusion

In this 20-year-old pregnant woman, cerebral metastatic choriocarcinoma was unsuspected prior to



craniotomy. Metastatic choriocarcinoma should be considered in any gravid female who presents with headache, seizure or other neurologic signs regardless of other symptomatic features. This case is particularly unusual in that it represents an example of choriocarcinoma coexistent with a first pregnancy where both

mother and child survived. Initial evaluation and close observation of a rapidly changing clinical picture allowed surgical intervention to carry this patient beyond her initial cerebral hemorrhage to receive the accepted treatment regimen.

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#### Effort to Elect Dr. Robert T. Kelly To AMA Board of Trustees Underway

Dr. John J. Regan of Minneapolis is chairman of the committee formed to elect Dr. Robert T. Kelly of Grand Rapids to the AMA Board of Trustees.

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Medical societies are encouraged to consider contributing to the election fund. Checks should be payable to the Committee to Elect Robert T. Kelly, M.D. and sent to the Minnesota Medical Association, 101 E. Fifth Street — Suite 900, St. Paul, Minnesota 55101.

#### Cover Photograph "Spring"

Dr. Bruce C. Nydahl, a Minneapolis internist, took the cover picture several years ago. These crocus buds appeared in his back yard very early one spring. The snow was still on the ground after a long winter, and even though spring had not yet arrived the heat of the sun brought forth these buds and made one think winter was at an end.

Dr. Nydahl is a graduate of the University of Minnesota Medical School and presently is a Clinical Assistant in the Department of Medicine at the University.

He has had covers on three previous issues of MINNESOTA MEDICINE: December, 1974, December 1977 and December 1978.

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# Aspergillosis of the Bronchus with Fruiting Bodies

IRENE P. POSALAKY, M.D.,\* RICHARD K. DYKOSKI, PA.,† DORIS S. SERSTOCK#

**A case of disseminated renal cell carcinoma with a rare form of fungal infection is presented. A grossly visible colonization of the fungus was found in the bronchus of the left lower lobe which revealed conidiophores ("fruiting bodies") pathognomic of *Aspergillus*. The lung parenchyma did not reveal any other fungus infection.**

**P**ULMONARY ASPERGILLOSIS is frequently seen as a terminal infection in patients dying of disseminated malignant disease. The inhaled spores often fail to germinate in the bronchial tree, but in severe cases the bronchial epithelium is destroyed and covered by a membrane consisting of fibrin, tissue debris, inflammatory cells, fungal mycelia and fruiting heads.<sup>4</sup>

The present case illustrates a bronchial surface infection with a grossly appreciable fungus growth of *Aspergillus fumigatus* in a patient with disseminated renal cell carcinoma without chemotherapy or antibiotic treatment.

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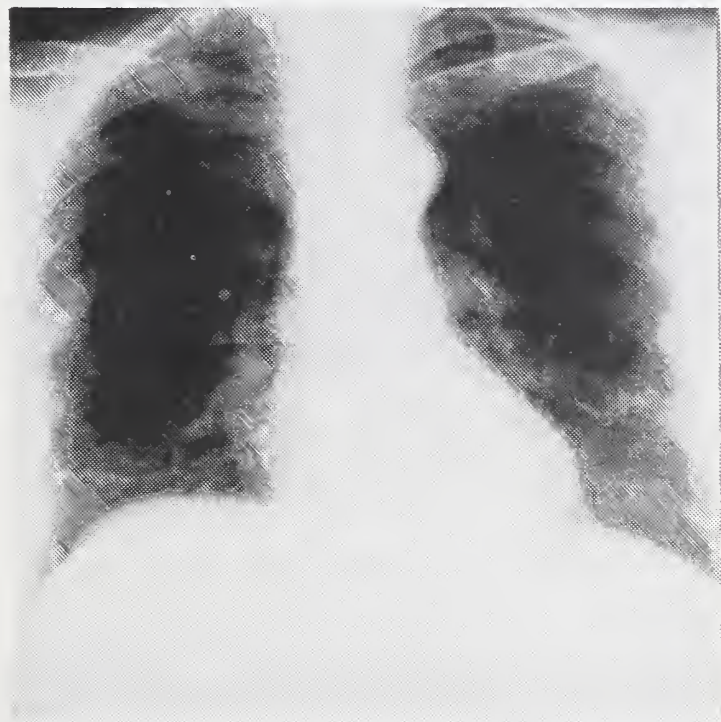


Fig. 1 — Chest Xray one week prior to death. There were no tumor nodules nor cavities.

## Case Report

A 54-year-old man was admitted to the hospital for evaluation of right sided hemiplegia, fever and weight loss. He had been well until six months prior to admission. Echogram of the kidneys revealed a large right kidney mass. Brain scan showed multiple intracerebral metastatic lesions. Bone marrow biopsy revealed metastatic adenocarcinoma. There were no metastatic lesions or cavitating lesions on the chest Xray (Figure 1). The patient received 3000 rads of radiation to his brain. His one month hospital course was that of a downhill trend.

## Autopsy Findings

The autopsy revealed a large necrotic renal cell carcinoma of the right kidney metastatic to ribs, vertebra, liver, pancreas, adrenal glands, and brain.

The lungs showed no gross tumor metastasis and no cavitating lesions or consolidation. The superior bronchus of the left lower lobe revealed a white plaque with a wooly growth of fungus (Figures 2 and 3). The underlying mucus membrane was congested and ulcerated. KOH preparation of the wooly material (Figure 4) revealed many conidiophores characteristic of *Aspergillus*. Cultures demonstrated



Fig. 2 — Orifice of the superior bronchus of the left lower lobe of the lung, showing a wooly growth of *Aspergillus fumigatus*. X3



the typical bluegreen mycelia with white borders at both 37°C and 25°C on Sabouraud's, dextrose agar as well as Czapek's confirmatory media characteristic of *Aspergillus fumigatus*.

Microscopic section of the bronchus disclosed a necrotizing process involving the mucosa and submucosal connective tissue. The fungus hyphae had invaded the deep tissue of the bronchial wall (Figure 5). There was an inflammatory reaction and congestion of capillaries with extravasation of erythrocytes. The lung parenchyma was free of the fungus infection.

### Comments

Patients with disseminated solid tumors are susceptible to saprophytic fungal growth.<sup>2,5</sup> The conidiophores of *Aspergillus* are found almost exclusively in the pulmonary cavities<sup>1</sup> and rarely as a surface infection of the bronchus.<sup>3,4</sup>

In reviewing 1000 consecutive autopsies between 1975-1978 it was found that 437 involved malignant tumors. Pulmonary aspergillosis was observed in four out of 54 cases of lymphomas and in four out of 382 cases of carcinoma. The only case revealing necrotizing mycotic bronchitis was associated with a parenchymal infection. None of the reviewed cases showed gross fungal colonization of the surface of the bronchus.



Fig. 3 — Close up of the fungus colony. X20

This case illustrates a very rare presentation of a mycotic bronchitis.



Fig. 4 — KOH preparation of wooly material, showing conidiophores of *aspergillus*. X650

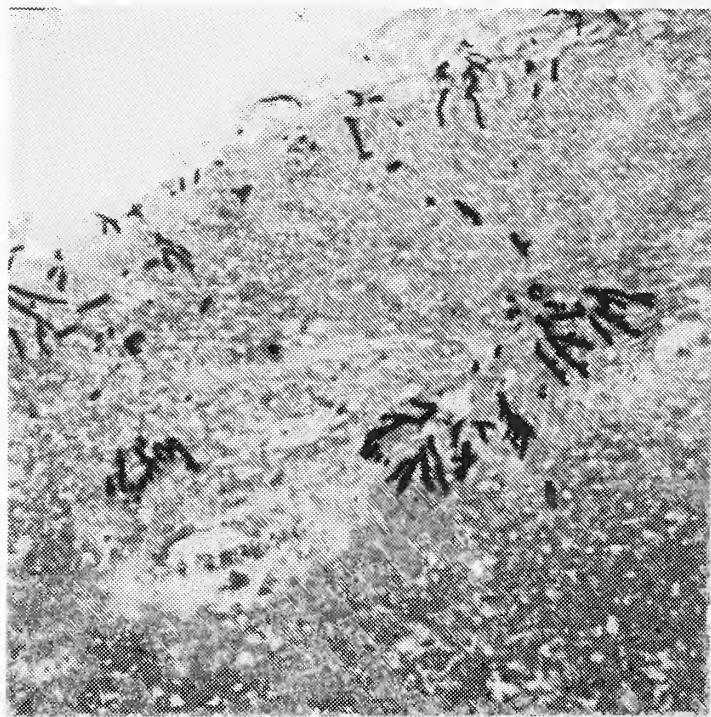


Fig. 5 — Section of the bronchial wall. Necrotizing bronchitis with invasion of septate hyphae into the connective tissue. Methamamine Silver Stain. X650

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# Immunology of Bladder Cancer

ALBERT J. MARIANI, M.D.,\* ROY E. RITTS, JR., M.D.,\* AND CHARLES C. RIFE, M.D.\*

From the immunologic standpoint bladder cancer has been the most extensively studied genitourinary malignancy. There is evidence for tumor protective as well as tumor destructive mechanisms. Early attempts at immunotherapy suggest cautious optimism, but until there is a better understanding of the interaction of the immune mechanisms with tumor clinical application will remain empirical.

**F**ROM THE IMMUNOLOGIC standpoint, bladder cancer has been the most extensively studied genitourinary malignancy. Immunotherapy of cancer is based upon the concept of immunologic surveillance which in its simple form states that the host's immunologic mechanisms recognize and destroy tumor cells arising *de novo* in normal tissues<sup>1</sup>. For tumor "rejection" to occur, there must be antigens which are recognized by the host as foreign to it. Animal studies suggest that tumors may, in fact, possess tumor specific antigens<sup>2</sup>. Cytotoxicity studies have demonstrated antigenic cross reactivity to chemically-induced bladder tumors in rodents<sup>3</sup>. A human tumor associated bladder tumor antigen was also thought to be demonstrated by microcomplement fixation<sup>4</sup>, but there is no definite evidence for human-tumor antigens. Unfortunately, the specificity of the above studies is uncertain because these same types of cytotoxicity studies demonstrate cytotoxicity to non-malignant as well as malignant tissues. Possibly, looking for specific tumor associated antigens is too simplistic conceptually and too difficult technically in that the surface antigens may be composed of tumor-specific antigens, viral-associated antigens, fetal antigens, as well as deletion of normal cell surface antigens<sup>5</sup>. There is further evidence that this surface antigen makeup may change as the tumor progresses<sup>6</sup>. Deletions of blood group antigens have been noted in patients with bladder cancer and were positively correlated with progression of disease<sup>7</sup>.

## Tumor Destructive Mechanisms

The principal antitumor immunologic mechanisms are thought to be cell mediated rather than humoral. Cytotoxicity to bladder tumor cell lines has been demonstrated<sup>8,9</sup>, but not found to be very specific to

the bladder tumors in that the cytotoxicity was also demonstrated against other benign and malignant conditions<sup>10-14</sup>. Although cell-mediated responses are probably the most important effectors of immunologic surveillance, there is also evidence of IgG humoral factors which enhance the cytotoxicity of T-lymphocytes against bladder tumor cell lines. Nevertheless, pathologists have long noted pronounced lymphoid reactions to middle-grade papillary bladder tumors<sup>15</sup> suggesting an *in vivo* host defense or reaction to these tumors.

A number of studies have demonstrated impaired cell-mediated responses in patients with bladder tumors, especially high-grade invasive ones. These impaired responses include: decreased reactivity of delayed hypersensitivity skin tests<sup>16-20</sup>, depressed lymphocyte blastogenic responses to phytohemagglutinin<sup>21</sup>, decreased numbers of T-lymphocytes<sup>22</sup> and an impaired leukocyte chemotactic response<sup>23</sup>. It is not clear whether these patients were immunologically compromised prior to oncogenesis and that this state prompted tumor growth or whether some activity of the tumor causes a depression of the immune response, although the latter case is probably correct.

## Tumor Protective Immune Mechanisms

While patients with intact cell-mediated responses were found to have increased survivals<sup>24-27</sup>, or at least increased interval survivals<sup>36</sup>, not all immunologic mechanisms are protective to the host. Studies have demonstrated the presence of blocking antibodies<sup>28</sup>, blocking antigen-antibody complexes<sup>29</sup>, blocking nonspecific regulatory globulins<sup>30,31</sup> and suppressor T cells<sup>32-34</sup>.

As if things were not complex enough, treatment modalities of radio and chemotherapy are not without their profound effects upon the immunocompetence of

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the host. Chemotherapeutic suppression is well known, and pelvic radiotherapy for invasive bladder tumor has been demonstrated to greatly reduce circulating T-lymphocytes<sup>35</sup>. In addition, anesthesia and major surgical procedures reduce circulating lymphocytes and depress all currently available measures of cell-mediated immunity<sup>36-38</sup>.

### Clinical Application of Immunotherapy

The rationale of immunotherapy is to enhance the immune mediated destruction of tumor either specifically (tumor-limited reactivity) or nonspecifically (all immune reactivity). While there have been attempts at immunotherapy since early in this century the first really promising results were obtained during the 1960s using contact sensitization with dinitrochlorobenzene and later intralesional challenge with dinitrochlorobenzene plus BCG against skin cancers that were refractory to other modalities of treatment. This work was done at Roswell Park in Buffalo and a 90% remission rate was claimed in 24 patients followed for seven to 10 years. Interestingly, not only were the primary lesions eradicated, but some distant metastatic lesions underwent inflammation and resolution presumably as a result of antitumor immune specificity. In a later, better controlled prospective study utilizing intralesional BCG against basal cell carcinoma, while the results were not as impressive, they were significant since 61% partial or complete remissions were attributable to the immunotherapy<sup>39</sup>.

BCG, which is an attenuated strain of bovine tuberculosis, has been demonstrated to arouse a brisk immune response from the host. It has been postulated that the mobilization of immunogenic cells results in an initial nonspecific inflammatory response as well as a secondary response to the tissue to which it was applied. In the case of tumor, this presumed specific reaction occurs through the liberation of tumor-associated antigens due to initial inflammatory response.

Experience with immunotherapy against genitourinary cancer is much less extensive. In a rather bold study, 16 patients with high grade metastatic bladder cancer were transfused with pig lymphocytes which were derived from pigs which had been sensitized to the tumor. Seven patients improved clinically and 14 out of 16 demonstrated an inflammatory response to the tumor<sup>40</sup>. A subsequent study further supported these findings<sup>41</sup>. To our knowledge this is the only study making an attempt to induce specific anti-bladder tumor immunity.

The other studies have used various forms of nonspecific immune modulators but the number of patients is quite small. For example, one patient with a single metastasis of malignant melanoma to the bladder was treated with intralesional BCG. Upon cystoscopic examination seven days later the lesion had been eradicated. This was confirmed by biopsy. The patient eventually succumbed to distant metastases<sup>42</sup>. In another study with a two-year followup, nine patients with superficial bladder tumors were treated by intradermal and intracavitary BCG. These patients had a significantly lower incidence of bladder tumor recurrence during the followup interval. All of these patients exhibited a cutaneous reaction to PPD<sup>43,44</sup>.

Tumor immunology research is rapidly moving ahead in centers world-wide. From previous studies we can suggest some guiding principles. It is clear that immunotherapy has not proven to be successful against large tumor burdens. It appears that it may be efficacious as an adjuvant treatment when tumor load is nil or minimal following other modalities of treatment. There are still a number of basic science and clinical questions to be resolved before immunotherapy can be applied rationally and routinely as part of our armamentarium against cancer. It is hoped that this will occur soon for medicine has historically been most successful when it has been able to stimulate the patients' own resources to combat disease.

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# The Cosmetic Surgery Patient

## Why do they do it to themselves?

JOHN G. STAFNE, M.D.\*

**Patients attempting to solve long standing personality problems by instant anatomical alterations is a familiar problem. They use the change in external appearance to solve inner problems.<sup>2</sup> Some psychiatrists have even equated cosmetic procedures as surgical psychotherapy.<sup>3</sup> Physicians dealing with potential cosmetic surgery patients should be aware of possible neurotic motivations. Supportive treatment may be indicated for patients with subjective or objective non-correctable deformities. The plastic surgeon has to be on constant guard not to use surgical procedures as a replacement for formal psychiatric counseling and/or treatment.**

**COSMETIC PATIENTS** think of themselves as ugly or defective, not ill. Reich, commenting on 750 patients seeking cosmetic surgery, concluded by his own evaluation that: 36% apparently had normal personality and realistic attitudes to an objective deformity, 62% of the patients had some emotional or personality trait disorder, while 2% could be categorized as psychotic.<sup>2</sup> Therefore many of these patients may seek the operation on the basis of neurotic or unrealistic motivations.

Patients are usually not seeking the removal of a symptom but the restoration of an ideal state that already exists in their imagination. Ambroise Pare is credited with the first written account of body image in the 16th century.<sup>3</sup> The body image is what an individual thinks of his physical features at any given time and therefore can be in a state of constant fluctuation.<sup>5</sup> This is determined by the actual sensory experience of what the patient or others see in themselves and the psychological factors with high emotional overtones.<sup>3,5</sup> The prepubertal patient, both male or female, usually has preconceived ideas of what his/her appearance will be following the secondary sexual changes. We see unmarred patients who are neurotics with low self-esteem and distorted body image who are very miserable and unhappy.<sup>3</sup>

Body parts with high priority value psychologically are the eyes, nose, breasts, and genitalia.<sup>3</sup> Physicians who may be consulted by potential cosmetic surgery patients should be more aware of the emotional factors motivating these patients to seek surgery.

### Rhinoplasty

As the nose is in full view at all times and very difficult to camouflage it assumes a special role in the

body image. The nose is an organ of secondary sexual characteristics.<sup>3,5</sup> The youngest patients seeking cosmetic surgery are usually teenage females requesting a rhinoplasty. In the post-pubertal female the appearance of a masculine nose may accentuate emotional problems in a patient who already has distortion of sexual identification.<sup>5</sup> The young female with her "father's nose" may be having anxieties of competition with her mother's beauty. She may be seeking powerful female aggressive weapons to fulfill the need of narcissistic power of compelling admiration from others or controlling men much like her mother does. If her mother is instrumental in seeking this surgery, the female patient may be sacrificing herself to her mother's perfectionism as in other areas of her life such as clothing etc. She may be seeking help in getting rid of her nasty disposition and bad temper.<sup>2</sup>

Sociological factors such as anti-ethnic problems or fear of meeting strangers may produce strong feelings of loneliness, isolation, and rejection.<sup>3</sup> These social anxieties may lead to long standing inferior feelings or complexes. The male seeking rhinoplasty may be in need of more self-assurance to help him through a crisis. His crooked nose may result in a body image of an undesirable. He may feel that this is a noticeable distraction in all his personal relationships, including employment. It is interesting that some males with the distorted nasal structures obtained in sports may wish to retain this deformity as a symbol of being a hero not unlike the facial saber scar.


### Mammoplasties

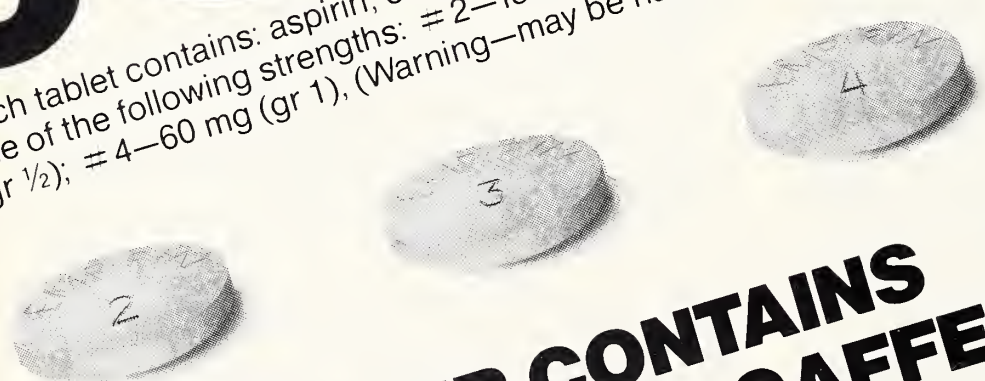
Women seeking augmentation mammoplasties may have reached a maturational crisis and are involved in a turning point in their lives. There may be a need for

\*Plastic surgeon, St. Paul, Minnesota.



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inner strength, confidence, and self-sufficiency. Principle aim may be more self-assertiveness, seeking personality transplants, or having failed in psychiatric therapy may be seeking surgical psychotherapy.<sup>1</sup> The patient may be having chronic dissatisfying relationships in her marriage. She may be seeking answers to fearful or competitive attitudes towards her husband. The augmentation patient probably is seeking the restoration of an ideal part that they feel deprived of including features they never had,<sup>1</sup> again relating to the prepubertal fantasy of future body image. Her basic aim, however, outwardly seems to become more attractive not only to herself but to others of both sexes. Women participating in an active sport such as tennis, golf and swimming truly have a difficult time of camouflaging their flat chest. This surgery may open a whole new world for her wearing apparel, and this in itself may give her more confidence in her femininity.

### Reduction Mammoplasties

Patients seeking reduction mammoplasties seem to have less complicated neurotic motivations.<sup>1</sup> The reduction of weight and obtaining a more youthful contour certainly leads to a more comfortable life. The patient seems to be rejuvenated by her more youthful body shape. However, in patients who have developed their macromastia or ptosis following pregnancies may have the inner conflicts usually of guilt associated with what their children have "done to her". In the young female seeking reductions, her anxieties again are reflected in her body image.<sup>1</sup> In our breast orientated society these young females have fantasized what their future feminine shape may be, based on photos etc. When they become "over-endowed" they may develop various emotional problems which they may compensate by becoming antisocial or even overweight to produce better body proportions.

### Reconstruction following Mastectomy

With the recent trend in modified radical mastectomy, reconstruction of the breast is now surgically and medically acceptable. Certainly the removal of the breast greatly reduces the confidence of a woman about her femininity and her sexual attractiveness.<sup>1</sup> She also may be going through the emotional strains of a possible early death leaving a young family motherless. She may foresee marital problems when she is less than the ideal sexual partner. This patient may also

restrict her social activity in sports not only because of the physical restrictions of her operation but her inability to dress properly. The post-mastectomy patient must be well-counseled on what to expect from any reconstructive procedure. Her mental visualization of the newly reconstructed breast does not even come close to the reality of the mound of tissue presented to her usually through multiple surgical procedures. She must be well-counseled to the fact that the plastic surgeon does not have the answer for everything.

### The Aging Face

Older patients who seek surgical relief of the signs of aging are in a period of their lives when other major sociological changes are quite common. Someone has referred to these patients as the post-adolescent rhinoplasty patient, only growing older.<sup>2</sup> These patients may have recently been bereaved by divorce or death, threatened by loss of children, or threatened by loss of professional status.<sup>1,4</sup> They are seeking rejuvenation, hopes of increased sexual attractiveness, and a youthful vigor and appearance.<sup>1</sup> Many of these patients are dealing with unresolved grief reactions.<sup>2,4</sup> They may have fears of isolation, abandonment, loss of love, loneliness, lack of friendship and fear of death.<sup>3</sup> They want to reestablish previous defense mechanisms such as denial and activity which are threatened by aging.<sup>2</sup> The nonworking patient is continually seeking to join organizations to occupy his/her time.<sup>4</sup> They wish to remove their evidence of sadness by a surgical procedure.

### Conclusion

This is an article of awareness, not treatment. These patients do not need to be told that they are crazy or to forget about it. Their emotional needs may be easily met with a primary physician's help. Some patients may need only simple supportive types of treatment; an offer to listen to them when the opportunity arises. Some patients may need formal counseling and/or psychiatric care. In times of a crisis a plastic surgery consultation may be helpful to give insight to emotional needs and what can be done surgically. However surgery itself must be delayed for at least six to twelve months to let their lives settle down. Some patients may be simply interested in information and in need of help in obtaining plastic surgery consultation.

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# Case Report

## Multiple Myeloma Terminating as Plasma Cell Leukemia and Coinciding with a Change in Light Chain Production

GARY L. GRAMMENS, PH.D, M.D.\*; and RONALD W. ELLIS, M.D.\*

**A 51-year-old female with plasma cell leukemia is described. Forty-two months prior to the onset of the leukemia; multiple myeloma was diagnosed with a IgG lambda monoclonal gammopathy characterized. With conventional treatment the gammopathy cleared, however, coinciding later with the emergence of the plasma cell leukemia a different IgG kappa gammopathy developed. This particular clinical observation has not been previously reported and appears to be very rare.**

**ACUTE** PLASMA cell leukemia is rare and accounts for no more than 3-5% of all cases of immunocytic dyscrasia. Furthermore for it to develop terminally in patients with prior multiple myeloma in whom this later diagnosis has been established for longer than three years is considerably rarer. A very unusual occurrence in the clinical course of myeloma is the emergence of a different monoclonal protein as a feature of relapse. We recently observed the simultaneous development of both these events in one patient. To our knowledge this has not been previously reported.

### Case Report

A 51-year-old female had back pain in December, 1973. In March, 1974 lytic lesions were observed in the lumbar spine, pelvis, both upper femurs, ribs, and skull. Anemia (Hb. 10.1 gm/100ml) and a 10 lb. weight loss also were recorded. A monoclonal peak in the pre-beta region was seen on the protein electrophoresis (total protein 7.1 gm/100ml) and identified as IgG of the lambda light chain type (1.3 gm/100ml). Free lambda light chains were present on two determinations in both urine and serum. Kappa light chains were looked for and were absent. IgA was 10 mg%; IgM was 20 mg%. A bone marrow aspirate showed 20% plasma cells with particles showing sheets of myeloma cells.

The patient was treated with monthly cycles of Melphalan and Prednisone until March, 1975, when the Prednisone was omitted and the Melphalan continued at 8 mg. daily for seven days on a monthly or bimonthly basis. With this treatment the patient's symptoms disappeared, the anemia corrected, and from June, 1974, the serum monoclonal spike was absent or present only in trace amounts. The lambda light chains were not found in either serum or urine.

In July, 1976, the patient developed leukopenia. In September, 1976, a posterior iliac spine bone marrow aspirate and bone core biopsy study showed moderate hypocellularity with no increase in plasma cells. Chemotherapy was then discontinued.

In July, 1977, the patient's hemoglobin was 12.2 gm%, white blood count 7,100, with a normal differential. In September, 1977, the patient complained of lower sternal bone pain. Serum protein electrophoresis detected a monoclonal spike merging into the beta region. It was further characterized as being IgG of the kappa light chain type. Free kappa chains were detected with monospecific antisera in both the serum and urine. Lambda light chains were repeatedly tested for and not detected. On September 27, 1977, the patient's hemoglobin was 9.8 mg%, white blood count 21,700. On October 6, 1977, the white blood count was 33,000 with the peripheral blood smear revealing 91% plasma cells of varying immaturity. A sternal bone marrow aspirate on October 6, 1977, was markedly hypercellular with nearly complete replacement of normal cells by malignant plasma cells. By light microscopy the cells were plasma-blasts with eccentric nuclei in a deep blue cytoplasm. Multinucleated forms and cytoplasmic vacuoles were also seen. Morphologically these cells differed from those present in the patient's bone marrow in 1974. Electron microscopic study of the patient's peripheral blood cells showed extensive rough endoplasmic reticulum, a prominent perinuclear Golgi zone, and the characteristic nuclear pattern of plasma cells. No Auer rods were found. Determination of the cytoplasmic immunoglobulins of these cells showed 56% of the mononuclear cells to have kappa light chain, 1% lambda light chain and the remainder neither. The serum muramidase level was 3.8 (normal 2-16).

On October 11, 1977, a cycle of COAP (Cyclophosphamide, Vincristine, Ara-C, Prednisone) was instituted. The patient's WBC was 2,500 on the 17th hospital day with the bone marrow then showing persistence of the malignant plasma cells. On the 18th hospital day another slightly abbreviated course of COAP and 75 mg. of Doxorubicin per day for two days was given. Profound, prolonged cytopenias occurred complicated by *Fusobacterium* and *Klebsiella* bacteremia. These were controlled with a combination antibiotics, WBC and Platelet transfusions; however, extensive mucous membrane candidiasis intervened. On the 32nd day the patient began experiencing dyspnea, and pulmonary infiltrates appeared. On the 36th day the bone marrow again showed only plasma cells. Progressive pulmonary distress occurred and the patient expired on the 39th hospital day. At autopsy multiple sections of bone marrow from ribs and sternum revealed virtually complete replacement by the malignant plasma cells. Developing RBCs,

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myeloid cells and megakaryocytes were almost completely absent. The lungs revealed extensive edema and hemorrhage. Masses of yeast-form fungi and pseudohyphae were found in the lungs, liver, spleen, kidney, and myocardium.

### Comment

The clinical course of our patient was distinguished by the almost simultaneous development of two different, although related, rarities: (1) Plasma cell leukemia (PCL) evolving from long standing, and apparently clinically stable, multiple myeloma (MM) and (2) with PCL heralded by a qualitative change in the paraprotein. This combination of circumstances, which to our knowledge has not been previously reported, offers a unique glimpse at a biological oddity.

Acute myelocytic and monocytic leukemia may be part of the natural history of MM as well as delayed consequence of chemotherapy for multiple myeloma.<sup>1</sup> PCL may be a similar infrequent complication of treatment, or possibly, a rare event in the natural history of myeloma. Moreover to occur in a patient with previously well established MM for more than 42 months is even rarer. Kyle reporting on a large series of patients with MM found 17 cases with PCL and estimated its incidence among patients with immunocytic dyscrasias at 1.6%.<sup>2</sup> More importantly, in only two of their 17 patients had the diagnosis of MM been established longer than one year before developing the leukemic picture. Pruzanski in a report of 10 cases with PCL reported one poorly documented case of "multiple myeloma or chronic lymphatic leukemia" which evolved into PCL after more than one year.<sup>3</sup> Woodruff reported on 15 cases of PCL in a population of 227 patients with plasma cell malignancy. Two percent of the patient population developed a terminal PCL phase but no mention was given as to when this developed in relation to the original diagnosis of MM.<sup>4</sup> No other large series of patients of PCL exists.

In MM the abnormal protein being produced almost always remains qualitatively constant throughout the clinical course. However, qualitatively different myeloma proteins occurring simultaneously in one patient have been reported. These simultaneous M components have been called "double myelomas" because of the presence of two different types of light chains, heavy chains or both.<sup>5-7</sup> It is felt that these "double myelomas" represent a biclonal gammopathy, but in at least one case a single clone of

plasma cells produced more than one kind of paraprotein.<sup>8</sup> In our patient the descriptive term "double myeloma" may not be appropriate; because with sensitive testing, both at the onset and terminally in the patient, we were unable to demonstrate the presence of two abnormal proteins. The term "changed myeloma" may be more correct, for it describes what occurred both serologically and clinically.

For total change in the paraprotein being produced to occur, any one of three situations might happen. First, the original clone of plasma cells switches protein synthesis to a different species. Second, a new clone, perhaps mutant from the original, begins its protein synthesis, and at about the same time the original clone ceases in its protein production. A third possibility is the presence of two malignant clones from the onset in which one clone is dedifferentiated or suppressed to the extent of being incapable of synthesizing a recognized protein. Later, perhaps by chemotherapeutically "selecting out", this resistant clone begins to produce its own unique protein.

It is impossible to definitely state which of these possibilities was occurring in our patient, however, certain observations can be made. Hobbs has stated that "biochemical dedifferentiation parallels more malignant dedifferentiation".<sup>9</sup> This case is *prima facie* evidence to support this, especially if the single clone hypothesis is true. If a clone not present at the onset were responsible for the manufacture of the kappa chains terminally in this patient, this, in fact, would represent the development of a *denovo* PCL coinciding with an already existing myeloma. Thus, in effect, two cases of an immunocytic dyscrasia in one person, a statistically possible but decidedly very rare event.

PCL is often fulminating and rapidly fatal disease whose mean survival time from diagnosis is two to 4.8 months.<sup>3,4</sup> Because a consistently effective form of treatment has not been described we were prompted by the success of one report using COAP.<sup>10</sup> Despite this aggressive combination plus the addition of Doxorubicin in the second cycle, the result was unsuccessful.

### Acknowledgment

The authors would like to express their thanks to Robert Rydell, MD for the electron microscopic studies, Manual Kaplan, MD for the cytoplasmic immunoglobulin studies, John Hetzler, MD for clinical pathology support and Nancy MacNaughton for secretarial assistance.

References will be found on page 209.



# Special Article

## Neuropathies of Diabetes Part II. Asymmetric Neuropathies †

DONALD ZIMMERMAN, M.D.\*

ALTHOUGH SYMMETRIC diabetic neuropathies may arise from generalized metabolic derangements, asymmetric forms appear to be produced by local vascular occlusion or by local trauma to vulnerable nerves. Both cranial and peripheral neuropathies may manifest an asymmetric pattern. The most common cranial neuropathies involve nerves to the extraocular muscles. Asymmetric neuropathies of peripheral nerves include mononeuropathy (including mononeuropathy multiplex), plexopathy (the most common lesion in diabetic amyotrophy), and radiculopathy.

### Cranial Neuropathies

#### *Incidence and Pathogenesis*

The most commonly affected cranial nerve is the oculomotor. Abducens and trochlear nerves are involved less frequently.<sup>1</sup> Involvement of nerves to extraocular muscles occurs in 1 to 5% of patients with neuropathy<sup>2,3</sup> and is usually found in patients who are more than 50 years old who have no other clinically evident neuropathy.<sup>1,4</sup> There is no relationship between the onset or the remission and the control of blood glucose level.<sup>1</sup> Pathologic study suggests that vascular occlusion due to microangiopathy may be the cause in these situations.<sup>5</sup>

#### *Diagnosis*

The clinical presentation of oculomotor nerve palsies includes diplopia in virtually all patients (some patients must manually raise the ptotic eyelid to detect the diplopia).<sup>1,6</sup> Headache is present in 55 to 80% of these patients compared with virtually 100% of patients who have ophthalmoplegia due to intracranial aneurysm. Headache usually begins at the same time as the diplopia and ptosis, although in 15 to 45% of patients, headache precedes other symptoms (interval varying from one to 21 days).<sup>1,6</sup> The pain is usually moderate (although it may be extremely intense) and most commonly remits within a few days.<sup>1</sup> Pain usually occurs within the distribution of the ipsilateral

ophthalmic division of the trigeminal nerve, and approximately 18% of patients with this distribution of symptoms have signs of trigeminal involvement (hypoesthesia of the cheek or absent corneal reflex).<sup>1</sup> As many as 30% of patients with diabetic oculomotor palsy have a history of Bell's palsy.<sup>6</sup>

Signs of external ophthalmoplegia may be mild or marked. Ninety percent of patients have ptosis. The pupillary dilation and unresponsiveness of oculomotor palsy is seen in only 20% of patients who have a diabetic cause<sup>1,6</sup> compared with 80% of patients who have tumor and 97% who have aneurysm.<sup>7</sup> In diabetic patients with pupillary involvement, iridoplegia is almost uniformly incomplete.<sup>1,7</sup> In addition to manifesting the features of excruciating pain and dense iridoplegia, aneurysmal ophthalmoplegia (which usually occurs in the setting of subarachnoid hemorrhage)<sup>8</sup> is characteristically associated with nuchal rigidity, disturbance of consciousness, and bloody cerebrospinal fluid.

Most clinicians use carotid angiography to rule out aneurysm in diabetic patients with pupillary involvement. Although signs of simultaneous involvement of more than one oculomotor nerve have been reported in diabetic ophthalmoplegia,<sup>2,9,10</sup> this pattern is rare.<sup>1,11</sup> If this combination is encountered in diabetic ketoacidosis, mucormycosis should be considered. Clues suggesting such a cause include pupillary involvement, chemosis, and proptosis. In addition to mucor, other infections as well as tumors may affect the cavernous sinus (compromising nerves III, IV, V, and VI) or the orbit (causing chemosis and proptosis). Roentgenograms of the skull, with additional views of the basilar and optic foramina, as well as tomograms of the orbit and sinuses, may help to exclude the possibility of a neoplastic process. Myasthenia gravis, a common cause of ophthalmoplegia in diabetic patients,<sup>1</sup> may be ruled out by means of the Tensilon (edrophonium) test. Graves' ophthalmopathy may be considered unlikely if forced ductions are normal. A normal erythrocyte sedimentation rate makes giant cell arteritis less likely.<sup>11</sup>

Abducens palsy is less than half as frequent as oculomotor palsy and is associated with pain in only

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†See Part I, February, 1980 issue of Minnesota Medicine 63:2:119, 1980.

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28% of patients.<sup>1</sup> In diabetic patients, trochlear nerve lesions are the least common of oculomotor nerve palsies. Both lesions (nerves VI and IV) should be evaluated in the same manner as the oculomotor lesions. All of these lesions resolve in weeks to months.

### Peripheral Neuropathies

#### *Mononeuropathy*

Diabetic mononeuropathy affecting peripheral nerves is far more frequent than oculomotor mononeuropathy.<sup>2</sup> The nerves that are most frequently involved are those most vulnerable to trauma — common peroneal, median, ulnar, lateral femoral cutaneous, and femoral nerves.<sup>12</sup> The treatment of these lesions with splints, braces, exercises, and surgery is similar for diabetic and nondiabetic patients.

#### *Diabetic Amyotrophy*

An asymmetric neuropathy that often has been mistakenly regarded as a peripheral mononeuropathy of the femoral nerve — diabetic amyotrophy — is now considered to occur in various anatomic patterns. Frequently, anterolateral leg muscles are involved in addition to those of the anterior aspect of the thigh. This pattern suggests a plexus lesion affecting multiple peripheral nerves.<sup>13,14</sup> The distribution of sensory loss suggests radiculopathy in some instances and mononeuritis multiplex in others.<sup>14,15</sup>

Diabetic amyotrophy affects diabetic patients in middle and old age. Diabetic control may be adequate or inadequate, and approximately one-third of amyotrophic patients have amyotrophy as the initial manifestation of diabetes.<sup>14</sup> The most commonly and severely affected site is the anterior aspect of the thigh. As many as 58% of patients have milder involvement of the upper extremity.<sup>14</sup> Pain (often described as burning with superimposed lancinating jolts) extends from the hip or low back to the affected thigh and is worse at night.<sup>15</sup> Quadriceps and iliopsoas muscles are weak and atrophic. Hamstrings are spared, and anterolateral calf muscles are variably involved.<sup>16</sup> Muscle fasciculations occur in approximately 25% of affected patients, and patellar reflexes are uniformly diminished on the involved side.<sup>14</sup> Sensory loss is usually limited to “background” sensory polyneuropathy of both lower extremities. Loss of sensation in the distribution of the femoral nerve is distinctly uncommon and suggests that the anatomic

level of involvement is usually proximal to the femoral nerve per se.<sup>14,17</sup> Plantar reflexes are extensor in approximately 17% of patients.<sup>14</sup> The protein level in the cerebrospinal fluid is elevated in approximately 50% of patients — in 25%, it exceeds 200 mg/dl.<sup>14</sup>

Therapy in amyotrophy includes symptomatic treatment of dysesthesias (amitryptiline and fluphenazine are useful), exercise (and splints if sequelae such as footdrop or wristdrop are present), and institution of tight metabolic control of diabetes. With improvement in the management of the blood glucose level, virtually all patients improve. During a period of months, pain tends to remit, although occasional aching may persist in as many as 20% of patients.<sup>14</sup> Fifty percent of patients lose the muscle atrophy entirely; and in approximately half of these, muscle strength returns to normal.<sup>14</sup>

#### *Radiculopathy*

Another radicular syndrome that has been described recently is truncal radiculopathy presenting as abdominal pain.<sup>18</sup> Three of four patients with this problem suffered pain over the vertebral column, in addition to anterior abdominal pain. The abdominal pain varied from a pressure sensation to burning or stabbing. Only two of the patients had detectable truncal sensory or motor signs. All four had evidence of neuropathy on electromyography of paraspinal muscles. A similar condition has been described as occurring over the thoracic portion of the trunk.<sup>19</sup> Patients with this syndrome should be treated symptomatically, and care should be taken to avoid unnecessary invasive procedures, such as abdominal exploration.

### Summary

The neuropathies of diabetes can be grouped into two forms: symmetric and asymmetric. The asymmetric form can be subdivided into cranial and peripheral types. The cranial type most commonly affects the nerve to the extraocular muscles and is associated with a good prognosis. This type must be differentiated from the more ominous causes of cranial nerve involvement. The peripheral forms most frequently involve single peripheral nerves, and the prognosis is the same as that for nondiabetic patients with similar involvement. The most characteristic type, however, is amyotrophy, which may arise at many different anatomic levels. The long-term prognosis for these patients generally is good.

References will be found on page 209.



# Minnesota Medical Association

## Static or Dynamic? Ethics and Change

GEORGE B. MARTIN, M.D.\* and WILLIAM JACOTT, M.D.†

Most of medicine knows that to stand still is impossible. Our behavior toward one another, our patients, and society has indeed changed. Since this is true, there is need for evaluation of our ethics.

These Principles of Medical Ethics are considered a set of guidelines governing our profession's behavior. Let us compare our present code and the proposed changes.

### AMA's Present Code

Preamble. These principles are intended to aid physicians individually and collectively in maintaining a high level of ethical conduct. They are not laws but standards by which a physician may determine the propriety of his conduct in his relationship with patients, with colleagues, with members of allied professions, and with the public.

Section 1. The principal objective of the medical profession is to render service to humanity with full respect to the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion.

Section 2. Physicians should strive continually to improve medical knowledge and skill, and should make available to their patients and colleagues the benefits of their professional attainments.

Section 3. A physician should practice a method of healing founded on a scientific basis; and he should not voluntarily associate professionally with anyone who violates this principle.

Section 4. The medical profession should safeguard the public and itself against physicians deficient in moral character or professional competence. Physicians should observe all laws, uphold the dignity and honor of the profession and accept its self-imposed disciplines. They should expose, without hesitation, illegal or unethical conduct of fellow members of the profession.

Section 5. A physician may choose whom he will serve. In an emergency, however, he should render

### Ad Hoc Committee's Proposed Development Plan

Preamble: This language establishes broad areas of responsibilities for all physicians, and reaffirms the belief that ethical standards are for the benefit of the patient. To allow for maximal individual discretion and accountability, these statements are clearly guidelines open to interpretation and universal application.

I. A concise statement of mission emphasizing the magnitude of a physician's commitment, and how it shall be met.

II. This wording is a clear mandate for self-discipline, calling on the precepts of fairness and honesty toward all. The deceitful are to be exposed, the impaired helped, and the unscientific educated.

III. Society should expect obedience to laws properly enacted, but the dedication of a physician requires lawful disagreement and attempts at modification of those laws inimical to sound patient care or contrary to accepted moral behavior.

IV. Due process is constitutionally guaranteed. No one has, or should have, the ability to abridge the legally given rights of another. Similarly the professional relationship is predicated on trust, and the confidentiality of this relationship, within the constraints of the law, must be assured.

V. Effective implementation of a physician's mission depends upon the application of sound scientific concepts, the ability of the public to make intelligent health choices, both as to procedure and person, and the liberal use of consultation with other health professions as may be indicated.

VI. Within the framework of these Principles, the

\*Chairman, MMA Speaker's Special Reference Committee on Medical Ethics.

†Co-chairman of the above committee.

See February 1980 issue, page 113, for previous article.



AMA's  
Present Code Continued

service to the best of his ability. Having undertaken the care of a patient, he may not neglect him; and unless he has been discharged he may discontinue his services only after giving adequate notice. He should not solicit patients.

Section 6. A physician should not dispose of his services under terms or conditions which tend to interfere with or impair the free and complete exercise of his medical judgment and skill or tend to cause a deterioration of the quality of medical care.

Section 7. In the practice of medicine a physician should limit the source of his professional income to medical services actually rendered by him, or under his supervision, to his patients. His fee should be commensurate with the services rendered and the patient's ability to pay. He should neither pay nor receive a commission for referral of patients. Drugs, remedies or appliances may be dispensed or supplied by the physician provided it is in the best interest of the patient.

Section 8. A physician should seek consultation upon request; in doubtful or difficult cases; or whenever it appears that the quality of medical service may be enhanced thereby.

Section 9. A physician may not reveal the confidences entrusted to him in the course of medical attendance, or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the individual or of the community.

Section 10. The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community.

Proposed Principles

Preamble: The medical profession has long subscribed to a body of ethical statements developed primarily for the benefit of those whom it serves. As a member of this profession, a physician must recognize responsibilities to society, to patients, to other health professionals and to self. The following principles adopted by the American Medical Association are not laws, but standards of conduct which define the essentials of honorable behavior for the physician.

- I. A physician shall be dedicated to providing medically competent service with compassion and respect for human dignity.

Ad Hoc Committee's  
Proposed Development Plan Continued

physician is entitled to certain rights which should not be denied if individual talents are to be developed to the fullest. Freedom of choice both by physician and patient is essential.

VII. Citizens should participate in community and societal affairs. By virtue of special training, a physician, as a citizen, may have additional value and should recognize that possibility. Whether to exercise that citizen's responsibility always has been and should remain an individual decision.



- II. A physician shall uphold the honor of the profession by dealing honestly with patients and colleagues and striving to expose those physicians deficient in character, competence, or who engage in fraud or deception.
- III. A physician shall respect the law, and also recognize a responsibility to seek changes in those requirements contrary to the best interests of the patient.
- IV. A physician shall respect the rights of patients, of colleagues, and of other health professionals, and shall safeguard patient confidences within the constraints of law.
- V. A physician shall continue to study, apply and advance scientific knowledge, make relevant information available to the public, and utilize the talents of other health professionals when indicated.
- VI. A physician, except in emergencies, shall be free to choose whom to serve, with whom to associate, and the environment in which to provide services consistent with appropriate patient care.
- VII. A physician, as a member of society, shall recognize a responsibility to participate in activities contributing to an improved community.

Please share your feelings with the Minnesota Medical Association's special reference committee on medical ethics during the annual meeting in May 1980.

Minnesota's delegation to the American Medical Association has a reputation of being dynamic, open, and encouraging change, because it represents an association that is not static, but constantly seeking improvement. Minnesota's physicians are not static. They are dynamic. We owe it to our peers and our patients to remain so.

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### **Continuing Medical Education** St. Paul Ramsey Medical Center

The Second *CLINICAL TOXICOLOGY* quarterly update conference will be held in the Amphitheater at St. Paul-Ramsey Medical Center on Wednesday, April 9, 1980. The guest speaker will be Dr. Frederick Lovejoy, Jr., Massachusetts Poison Control System and Chairman of the American Board of Medical Toxicology, Inc. The subject of his talk will be "Poisoning by Household Products".

These conferences qualify for Category I CME credits. They are sponsored by the Emergency Medicine Department at St. Paul-Ramsey Medical Center and the University of Minnesota Medical School under the direction of Dr. Kusum Saxena. For further information please contact: Carol Wolf at (612) 221-3311.



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### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** **Cardiovascular:** Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Central Nervous System:** Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. **Gastrointestinal:** Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. **Allergic:** Urticaria, rash, ecchymosis, erythema. **Endocrine:** Impotence, changes in libido, gynecomastia, menstrual upset. **Hematopoietic System:** Bone marrow depression, agranulocytosis, leukopenia. **Miscellaneous:** A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine<sup>®</sup>) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

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# Merrell



## Pulmonary Function in Healthy Minnesota Children Forced Expiratory Flow Volume Studies

WARREN J. WARWICK, M.D.\*

Normal values for forced expiratory flow volume curves from healthy Minnesota children are presented as useful to estimate small airway functioning.

**F**ORCED EXPIRATORY FLOW volume curves (FEFVC) were obtained simultaneously with the volume-time and flow-time curves during our study of 972 healthy white Minnesota school-aged children from a large suburban city with a low level of air pollution. This report establishes normal data for three specific measurements from these curves and twelve of their relationships.

### Experimental Plans

The participants, their mode of selection, the background information, the equipment used and the techniques of testing and analysis were described in the earlier paper on normal spirometric values.<sup>1</sup>

The decision to use an x-y recorder for preparing the on-line graph of the forced expiratory flow volume curve was made on the basis of economy and simplicity. Although all of the models we tested from four manufacturers gave similar results in the last half of the F-V curve, the Hewlett Packard Model 7045 A x-y recorder had the fastest response time, 76 cm/sec.

In an attempt to compare the speed of the HP 7045 A x-y recorder with an oscilloscope, we recorded several FEFVC on a high fidelity Tonnenberg FM recorder and replayed these recordings at a 16-fold reduction in speed, i.e., equivalent to a 16-fold increase in the response time of the recorder. When the regular and the amplified response curves were compared, the peak flow rate was found to be 6 percent low and 45 percent delayed, the vital capacity (VC) was identical, the flow rate at 50 percent expired vital capacity (MEF<sub>50</sub>) was 3 percent high and the flow rate at 75 percent expired vital capacity (MEF<sub>75</sub>) was 2 percent high. Because the

error inherent in the measurement of these parameters is at least 5 percent, all measurements during the last half of the VF curve were accepted at their recorded values. Therefore, the formulae and tables presented can be used with an oscilloscope as well as with a fast response x-y recorder without adjustment.

Table 1 contains the formulae for all of the FEFVC tests for both males and females.

In Table 2 for females and Table 3 for males, normal values for the four specific points (P.F., MEF<sub>50</sub>, MEF<sub>75</sub>, and TF) and for the 12 special relationships are tabulated.

Although the MEF<sub>50</sub>, the MEF<sub>75</sub> and the 12 special studies are arbitrary parameters, they are easy to measure and are potentially useful in assessment of small airway function.

### Peak Flow (PF<sub>s</sub>)

The peak flow rate (1 sec<sup>-1</sup>) used in two of the new pulmonary function tests is the peak flow rate measured from the spirometer, PF<sub>s</sub><sup>1</sup>, not from the recorder because the latter averaged 6 percent low. Use of PF<sub>s</sub> makes these new tests useful to laboratories using an oscilloscope, or recorded and reduced speed playback of data on a mechanical x-y recorder, as well as to laboratories using mechanical x-y recorders on line.

### Maximum Expiratory Flow Rate at 50 percent Expired Vital Capacity (MEF<sub>50</sub>)

This is the maximum flow rate (1 sec<sup>-1</sup>) at the instant when ½ of the forced vital capacity is expired. Although this test is independent of effort, in that the physiological limit for an individual cannot be increased by effort, it is altered by less than maximum effort to completely empty the lungs. Failure to completely empty the lungs will move the mid-point of the VC towards the peak flow and give too high a

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value. A reduced  $MEF_{50}$  indicates obstruction to air flow in small airways.

#### Maximum Expiratory Flow Rate at 75 percent Expired Vital Capacity ( $MEF_{75}$ )

This is the maximum flow rate ( $1 \text{ sec}^{-1}$ ) at the instant when  $3/4$  of the vital capacity is expired. It is independent of maximum effort in the same way as the  $MEF_{50}$ . It also suffers from failure to completely empty the lungs in a VC maneuver in that the point of  $3/4$  emptiness is moved towards the peak flow giving a falsely high value. A reduced  $MEF_{75}$  also indicates obstruction to air flow in the small airways.

The  $MEF_{75}$ , the  $MEF_{50}$ , and  $FET^1$  and  $AF^1$  all change in the presence of obstruction to air flow in the small airways. Since neither the size of the airways nor the generation of branching measured by each of these measurements is known, and since all are extremely sensitive but relatively less reproducible than the older tests of pulmonary function, they are best used as a group to estimate the severity of and changes in the obstruction to air flow in small airways.

#### Terminal Flow (TF)

Terminal flow ( $1 \text{ sec}^{-1}$ ) is the instantaneous flow rate at the moment the expiratory volume ceases to increase. The normal TF,  $0.0 \text{ l sec}^{-1}$ , occurs in 90 percent of children.

The meaning of a positive TF is unclear. Is it a variant of normal, or a sign of lung disease in otherwise normal children? Whatever, it may be interpreted as the flow rate at the time of premature closure of the trachea during the forced expiratory maneuver. It deserves to be noted, quantified when it is present, and analyzed along with other tests such as residual volume before firm guidelines can be given for its interpretation. In the meantime, it may be suspected as due to an instability of the trachea under high intrathoracic pressure at low lung volumes and, in the absence of other signs of lung disease, should not be regarded as of pathological importance.

Slope of the expiratory flow rate between 50 and 75 percent expired vital capacity ( $SEF_{50-75}$ )

Slope of the expired flow rate between 75 and 100 percent expired vital capacity ( $SEF_{75-100}$ )

TABLE 1

Pulmonary Function Test	Sex	Regression Equation Against Height (H) in centimeters	Standard Deviation in Percent	Rho
$PF_s^*$	M	$1n PF = 2.4991 \text{ lnH} - 10.7758$	16	0.93
	F	$1n PF = 2.4369 \text{ lnH} - 10.5350$	15	0.91
$MEF_{50}$	M	$1n MEF_{50} = 2.1326 \text{ lnH} - 9.3589$	16	0.78
	F	$1n MEF_{50} = 2.1958 \text{ lnH} - 9.6458$	14	0.77
$MEF_{75}$	M	$1n MEF_{75} = 2.1534 \text{ lnH} - 10.2213$	16	0.74
	F	$1n MEF_{75} = 2.2961 \text{ lnH} - 10.8666$	14	0.69
TF	M	$1n TF = .1858 \text{ lnH} - 2.7186$	14	0.05
	F	$1n TF = 1.2367 \text{ lnH} - 7.6627$	13	0.25
$SEF_{50-75} \left[ \frac{4(MEF_{50} - MEF_{75})}{\div VC} \right]$	M	$1n (SEF_{50-75}) = -0.8855 \text{ lnH} + 5.4196$	16	0.30
	F	$1n (SEF_{50-75}) = -0.6881 \text{ lnH} + 4.4813$	14	0.17
$SEF_{75-100} \left[ \frac{4(MEF_{75} - TF)}{\div VC} \right]$	M	$1n (SEF_{75-100}) = -.7380 \text{ lnH} + 4.5832$	16	0.35
	F	$1n (SEF_{75-100}) = -0.4556 \text{ lnH} + 3.3285$	14	0.16
$SEF_{50-100} \left[ \frac{2(MEF_{50} - TF)}{\div VC} \right]$	M	$1n (SEF_{50-100}) = -0.8241 \text{ lnH} + 5.0936$	16	0.43
	F	$1n (SEF_{50-100}) = -0.6810 \text{ lnH} + 4.4964$	14	0.32
$PF - MEF_{50}$	M	$1n (PF - MEF_{50}) = 3.8905 \text{ lnH} - 19.9816$	16	0.45
	F	$1n (PF - MEF_{50}) = 4.2334 \text{ lnH} - 21.8431$	14	0.41
$(PF - MEF_{50}) \div MEF_{50}$	M	$1n (PF - MEF_{50}) \div MEF_{50} = 1.7432 \text{ lnH} - 10.5435$	16	0.20
	F	$1n (PF - MEF_{50}) \div MEF_{50} = 2.0517 \text{ lnH} - 12.2553$	14	0.20
$MEF_{50} \div PF$	M	$1n (MEF_{50}) \div PF = -0.2646 \text{ lnH} + 1.0866$	16	0.20
	F	$1n (MEF_{50}) \div PE = -0.2448 \text{ lnH} + 1.0146$	14	0.19
$PF - MEF_{75}$	M	$1n (PF - MEF_{75}) = 2.5845 \text{ lnH} - 11.8841$	16	0.83
	F	$1n (PF - MEF_{75}) = 2.8430 \text{ lnH} - 13.2466$	14	0.65
$(PF - MEF_{75}) \div MEF_{75}$	M	$1n (PF - MEF_{75}) = .4323 \text{ lnH} - 1.6687$	16	0.15
	F	$1n (PF - MEF_{75}) = .5469 \text{ lnH} - 2.3800$	14	0.11
$MEF_{75} \div PF$	M	$1n (MEF_{75}) \div PF = -0.2425 \text{ lnH} + 0.2179$	16	0.14
	F	$1n (MEF_{75}) \div PF = -0.1446 \text{ lnH} - 0.2062$	14	0.06
$MEF_{50} - MEF_{75}$	M	$1n (MEF_{50} - MEF_{75}) = 2.1263 \text{ lnH} - 10.0159$	16	0.60
	F	$1n (MEF_{50} - MEF_{75}) = 2.2539 \text{ lnH} - 10.6934$	14	0.49
$(MEF_{50} - MEF_{75}) \div MEF_{75}$	M	$1n (MEF_{50} - MEF_{75}) = -0.05705 \text{ lnH} + 0.3585$	16	0.02
	F	$1n (MEF_{50} - MEF_{75}) = -0.07268 \text{ lnH} + 0.3301$	14	0.02
$MEF_{50} \div MEF_{75}$	M	$1n (MEF_{50} \div MEF_{75}) = -0.02087 \text{ lnH} + .8624$	16	0.01
	F	$1n (MEF_{50} \div MEF_{75}) = -0.10029 \text{ lnH} + 1.2208$	14	0.05

\*Peak flow obtained from the spirometer.



Slope of the expired flow rate between 50 and 100 percent expired vital capacity ( $SEF_{50-100}$ )

These three tests estimate the rate of change of the forced expiratory flow rate as the end of the vital capacity is reached. All are negative indicating a continuous decrease in flow rate with increasing volume expired. All the slopes increase, (approach 0), in the presence of obstruction to air flow in small

airways. These tests deserve study because they may be more sensitive or more specific for small airway disturbances than the  $MEF_{50}$  or  $MEF_{75}$  from which they are derived.

$$PF - MEF_{50}$$

$$(PF - MEF_{50}) \div MEF_{50}$$

$$MEF_{50} \div PF$$

TABLE 2  
Flow — Volume Curve Pulmonary Function Normal Values for Minnesota Children  
(Females height 90-178 cm)

Height	PF 1 sec <sup>-1</sup>	MEF 50 1 sec <sup>-1</sup>	MEF 75 sec <sup>-1</sup>	TF 1 sec <sup>-1</sup>	SEF 50 - 75 sec <sup>-1</sup>	SEF 75 - 100 sec <sup>-1</sup>	SEF 50 - 100 sec <sup>-1</sup>	PF - MEF 50 1 sec <sup>-1</sup>	(PF - MEF 50) MEF 50	MEF 50 PF	PF - MEF 75 1 sec <sup>-1</sup>	(PF - MEF 75) MEF 75	MEF 75 PF	MEF 50 - MEF 75 1 sec <sup>-1</sup>	MEF 50 - MEF 75 MEF 75	MEF 50 MEF 75
90	1.54	1.27	.59	.12	3.99	3.59	4.19	.06	.05	.92	.64	1.08	.42	.58	1.00	2.16
92	1.62	1.33	.62	.13	3.93	3.56	4.12	.07	.05	.91	.68	1.10	.42	.61	1.00	2.15
94	1.71	1.39	.65	.13	3.88	3.52	4.06	.07	.05	.91	.72	1.11	.42	.64	1.00	2.15
96	1.80	1.46	.68	.13	3.82	3.49	4.01	.08	.06	.90	.76	1.12	.42	.67	1.00	2.14
98	1.89	1.53	.71	.14	3.77	3.45	3.95	.09	.06	.90	.81	1.14	.42	.70	1.00	2.14
100	1.99	1.59	.75	.14	3.72	3.42	3.90	.10	.06	.89	.86	1.15	.42	.73	1.00	2.14
102	2.09	1.67	.78	.14	3.67	3.39	3.85	.10	.06	.89	.91	1.16	.42	.76	.99	2.13
104	2.19	1.74	.82	.15	3.62	3.36	3.79	.11	.07	.88	.96	1.17	.42	.80	.99	2.13
106	2.29	1.81	.85	.15	3.57	3.33	3.75	.12	.07	.88	1.01	1.19	.41	.83	.99	2.12
108	2.40	1.89	.89	.15	3.52	3.30	3.70	.13	.07	.88	1.07	1.20	.41	.87	.99	2.12
110	2.51	1.97	.93	.16	3.48	3.28	3.65	.14	.07	.87	1.12	1.21	.41	.91	.99	2.12
112	2.62	2.04	.97	.16	3.44	3.25	3.61	.15	.08	.87	1.18	1.22	.41	.94	.99	2.11
114	2.74	2.13	1.01	.16	3.40	3.22	3.56	.17	.08	.87	1.24	1.23	.41	.98	.99	2.11
116	2.85	2.21	1.05	.17	3.35	3.20	3.52	.18	.08	.86	1.31	1.25	.41	1.02	.98	2.10
118	2.98	2.29	1.09	.17	3.32	3.17	3.48	.19	.08	.86	1.37	1.26	.41	1.06	.98	2.10
120	3.10	2.38	1.13	.18	3.28	3.15	3.44	.21	.09	.85	1.44	1.27	.41	1.10	.98	2.10
122	3.23	2.47	1.18	.18	3.24	3.13	3.40	.22	.09	.85	1.51	1.28	.41	1.14	.98	2.09
124	3.36	2.56	1.22	.18	3.20	3.10	3.37	.24	.09	.85	1.58	1.29	.41	1.19	.98	2.09
126	3.49	2.65	1.27	.19	3.17	3.08	3.33	.25	.10	.84	1.65	1.30	.40	1.23	.98	2.09
128	3.63	2.74	1.32	.19	3.14	3.06	3.29	.27	.10	.84	1.73	1.31	.40	1.27	.98	2.08
130	3.77	2.84	1.36	.19	3.10	3.04	3.26	.29	.10	.84	1.81	1.33	.40	1.32	.98	2.08
132	3.91	2.93	1.41	.20	3.07	3.02	3.23	.31	.11	.83	1.89	1.34	.40	1.37	.98	2.08
134	4.06	3.03	1.46	.20	3.04	3.00	3.19	.33	.11	.83	1.97	1.35	.40	1.41	.97	2.07
136	4.21	3.13	1.51	.20	3.01	2.98	3.16	.35	.11	.83	2.05	1.36	.40	1.46	.97	2.07
138	4.36	3.23	1.56	.21	2.98	2.96	3.13	.37	.12	.83	2.14	1.37	.40	1.51	.97	2.07
140	4.51	3.34	1.62	.21	2.95	2.94	3.10	.40	.12	.82	2.23	1.38	.40	1.56	.97	2.07
142	4.61	3.44	1.67	.22	2.92	2.92	3.07	.42	.12	.82	2.32	1.39	.40	1.61	.97	2.06
144	4.84	3.55	1.72	.22	2.89	2.90	3.04	.45	.13	.82	2.42	1.40	.40	1.66	.97	2.06
146	5.00	3.66	1.78	.22	2.86	2.88	3.01	.47	.13	.81	2.51	1.41	.40	1.71	.97	2.06
148	5.17	3.77	1.84	.23	2.84	2.86	2.98	.50	.14	.81	2.61	1.42	.40	1.77	.97	2.05
150	5.34	3.88	1.89	.23	2.81	2.85	2.96	.53	.14	.81	2.71	1.43	.39	1.82	.97	2.05
152	5.52	4.00	1.95	.23	2.79	2.83	2.93	.56	.14	.81	2.82	1.44	.39	1.88	.97	2.05
154	5.69	4.11	2.01	.24	2.76	2.81	2.90	.59	.15	.80	2.93	1.45	.39	1.93	.96	2.05
156	5.88	4.23	2.07	.24	2.74	2.79	2.88	.63	.15	.80	3.04	1.46	.39	1.99	.96	2.04
158	6.06	4.35	2.13	.25	2.71	2.78	2.85	.66	.15	.80	3.15	1.47	.39	2.05	.96	2.04
160	6.25	4.48	2.20	.25	2.69	2.76	2.83	.70	.16	.80	3.26	1.49	.39	2.11	.96	2.04
162	6.44	4.60	2.26	.25	2.67	2.75	2.81	.74	.16	.79	3.38	1.50	.39	2.17	.96	2.04
164	6.64	4.72	2.32	.26	2.64	2.73	2.78	.78	.17	.79	3.50	1.51	.39	2.23	.96	2.03
166	6.84	4.85	2.39	.26	2.62	2.72	2.76	.82	.17	.79	3.62	1.52	.39	2.29	.96	2.03
168	7.04	4.98	2.46	.27	2.60	2.70	2.74	.86	.18	.79	3.75	1.53	.39	2.35	.96	2.03
170	7.25	5.11	2.52	.27	2.58	2.69	2.72	.90	.18	.78	3.88	1.54	.39	2.42	.96	2.03
172	7.45	5.25	2.59	.27	2.56	2.67	2.69	.95	.18	.78	4.01	1.55	.39	2.48	.96	2.02
174	7.67	5.38	2.66	.28	2.54	2.66	2.67	1.00	.19	.78	4.14	1.55	.39	2.55	.96	2.02
176	7.88	5.52	2.73	.28	2.52	2.65	2.65	1.05	.19	.78	4.28	1.56	.39	2.61	.96	2.02
178	8.10	5.66	2.81	.29	2.50	2.63	2.63	1.10	.20	.78	4.42	1.57	.38	2.68	.95	2.02



TABLE 3  
Flow — Volume Curve Pulmonary Function Normal Values for Minnesota Children  
(Males 90-188 cm)

Height	PF 1 sec <sup>-1</sup>	MEF 50 1 sec <sup>-1</sup>	MEF 75 1 sec <sup>-1</sup>	TF 1 sec <sup>-1</sup>	SEF 50 - 75 sec <sup>-1</sup>	SEF 75 - 100 sec <sup>-1</sup>	SEF 50 - 100 sec <sup>-1</sup>	PF - MEF 50 1 sec <sup>-1</sup>	(PF - MEF 50) MEF 50	MEF 50 PF	PF - MEF 75 1 sec <sup>-1</sup>	PF - MEF 75 MEF 75	MEF 75 PF	MEF 50 - MEF 75 1 sec <sup>-1</sup>	MEF 50 - MEF 75 MEF 75	MEF 50 MEF 75
90	1.60	1.27	.59	.15	4.20	3.53	4.00	.08	.07	.90	.78	1.32	.42	.64	1.11	2.16
92	1.69	1.33	.62	.15	4.12	3.48	3.92	.09	.07	.90	.82	1.33	.42	.67	1.11	2.16
94	1.78	1.39	.65	.15	4.04	3.42	3.86	.10	.07	.89	.87	1.34	.41	.70	1.10	2.15
96	1.87	1.45	.68	.15	3.97	3.37	3.79	.11	.08	.89	.92	1.36	.41	.73	1.10	2.15
98	1.97	1.52	.71	.15	3.89	3.32	3.73	.12	.08	.88	.97	1.37	.41	.77	1.10	2.15
100	2.08	1.59	.74	.16	3.83	3.27	3.66	.13	.08	.88	1.02	1.38	.41	.80	1.10	2.15
102	2.18	1.66	.77	.16	3.76	3.22	3.60	.14	.08	.87	1.07	1.39	.41	.83	1.10	2.15
104	2.29	1.73	.80	.16	3.69	3.18	3.55	.15	.09	.87	1.13	1.40	.40	.87	1.10	2.15
106	2.40	1.80	.84	.16	3.63	3.13	3.49	.16	.09	.86	1.18	1.42	.40	.90	1.10	2.15
108	2.52	1.87	.87	.16	3.57	3.09	3.44	.17	.09	.86	1.24	1.43	.40	.94	1.10	2.15
110	2.63	1.95	.91	.16	3.52	3.05	3.39	.18	.10	.85	1.30	1.44	.40	.98	1.09	2.15
112	2.76	2.02	.94	.16	3.46	3.01	3.34	.20	.10	.85	1.36	1.45	.40	1.02	1.09	2.15
114	2.88	2.10	.98	.16	3.41	2.97	3.29	.21	.10	.85	1.43	1.46	.39	1.06	1.09	2.15
116	3.01	2.18	1.02	.16	3.35	2.93	3.24	.23	.10	.84	1.49	1.47	.39	1.10	1.09	2.15
118	3.14	2.26	1.05	.16	3.30	2.89	3.20	.24	.11	.84	1.56	1.48	.39	1.14	1.09	2.14
120	3.27	2.34	1.09	.16	3.26	2.86	3.15	.26	.11	.84	1.63	1.49	.39	1.18	1.09	2.14
122	3.41	2.43	1.13	.16	3.21	2.82	3.11	.27	.11	.83	1.70	1.50	.39	1.22	1.09	2.14
124	3.55	2.51	1.17	.16	3.16	2.79	3.07	.29	.12	.83	1.77	1.51	.39	1.26	1.09	2.14
126	3.78	2.60	1.21	.16	3.12	2.76	3.03	.31	.12	.82	1.85	1.53	.38	1.31	1.09	2.14
128	3.85	2.69	1.26	.16	3.07	2.72	2.99	.33	.12	.82	1.93	1.54	.38	1.35	1.09	2.14
130	4.00	2.78	1.30	.16	3.03	2.69	2.95	.35	.13	.82	2.01	1.55	.38	1.40	1.08	2.14
132	4.15	2.87	1.34	.16	2.99	2.66	2.91	.37	.13	.81	2.09	1.56	.38	1.44	1.08	2.14
134	4.31	2.96	1.39	.16	2.95	2.63	2.88	.40	.13	.81	2.17	1.57	.38	1.49	1.08	2.14
136	4.48	3.06	1.43	.16	2.91	2.61	2.84	.42	.14	.81	2.25	1.58	.38	1.54	1.08	2.14
138	4.64	3.15	1.48	.16	2.88	2.58	2.81	.44	.14	.80	2.34	1.59	.38	1.59	1.08	2.14
140	4.81	3.25	1.52	.17	2.84	2.55	2.78	.47	.15	.80	2.43	1.60	.38	1.63	1.08	2.14
142	4.99	3.35	1.57	.17	2.80	2.52	2.74	.50	.15	.80	2.52	1.61	.37	1.68	1.08	2.14
144	5.16	3.45	1.62	.17	2.77	2.50	2.71	.52	.15	.80	2.61	1.62	.37	1.74	1.08	2.14
146	5.34	3.56	1.67	.17	2.74	2.47	2.68	.55	.16	.79	2.71	1.63	.37	1.79	1.08	2.13
148	5.53	3.66	1.72	.17	2.70	2.45	2.65	.58	.16	.79	2.80	1.64	.37	1.84	1.08	2.13
150	5.72	3.77	1.77	.17	2.67	2.42	2.62	.61	.16	.79	2.90	1.64	.37	1.89	1.08	2.13
152	5.91	3.88	1.82	.17	2.64	2.40	2.59	.65	.17	.78	3.00	1.65	.37	1.95	1.07	2.13
154	6.11	3.99	1.87	.17	2.61	2.38	2.57	.68	.17	.78	3.11	1.66	.37	2.00	1.07	2.13
156	6.31	4.10	1.92	.17	2.58	2.35	2.54	.72	.18	.78	3.21	1.67	.37	2.06	1.07	2.13
158	6.51	4.21	1.98	.17	2.55	2.33	2.51	.75	.18	.78	3.32	1.68	.36	2.11	1.07	2.13
160	6.72	4.32	2.03	.17	2.52	2.31	2.49	.79	.18	.77	3.43	1.69	.36	2.17	1.07	2.13
162	6.93	4.44	2.08	.17	2.50	2.29	2.46	.83	.19	.77	3.54	1.70	.36	2.23	1.07	2.13
164	7.15	4.56	2.14	.17	2.47	2.27	2.44	.87	.19	.77	3.66	1.71	.36	2.29	1.07	2.13
166	7.37	4.68	2.20	.17	2.44	2.25	2.41	.91	.20	.77	3.77	1.72	.36	2.35	1.07	2.13
168	7.59	4.80	2.25	.17	2.42	2.23	2.39	.95	.20	.76	3.89	1.73	.36	2.41	1.07	2.13
170	7.82	4.92	2.31	.17	2.39	2.21	2.37	1.00	.20	.76	4.01	1.74	.36	2.47	1.07	2.13
172	8.05	5.05	2.37	.17	2.37	2.19	2.34	1.05	.21	.76	4.13	1.75	.36	2.53	1.07	2.13
174	8.29	5.17	2.43	.17	2.34	2.17	2.32	1.09	.21	.76	4.26	1.75	.36	2.60	1.07	2.13
176	8.53	5.30	2.49	.17	2.32	2.15	2.30	1.14	.22	.75	4.39	1.76	.35	2.66	1.07	2.13
178	8.77	5.43	2.55	.17	2.30	2.14	2.28	1.20	.22	.75	4.52	1.77	.35	2.72	1.06	2.13
180	9.02	5.56	2.62	.17	2.27	2.12	2.26	1.25	.23	.75	4.65	1.78	.35	2.79	1.06	2.13
182	9.27	5.69	2.68	.17	2.25	2.10	2.24	1.30	.23	.75	4.79	1.79	.35	2.86	1.06	2.13
184	9.53	5.83	2.74	.17	2.23	2.08	2.22	1.36	.23	.75	4.92	1.80	.35	2.92	1.06	2.12
186	9.79	5.96	2.81	.17	2.21	2.07	2.20	1.42	.24	.74	5.06	1.81	.35	2.99	1.06	2.12
188	10.05	6.10	2.87	.17	2.19	2.05	2.18	1.48	.24	.74	5.20	1.81	.35	3.06	1.06	2.12



These three tests are altered by factors that reduce the instantaneous flow of air at any place in the FEFVC from the PF to the  $MEF_{50}$ . Although the three tests will vary together which will be the most sensitive or specific awaits careful evaluation. The absolute values of the PF —  $MEF_{50}$  and the  $(PF - MEF_{50}) \div MEF_{50}$  will increase and the  $MEF_{50} \div PF$  will decrease when the air flow obstruction is more severe in the small airways than in the trachea and large bronchi, and will reverse when air flow obstruction in the trachea and larger airways is relatively greater than in the small airways.

$$PF - MEF_{75}$$

$$(PF - MEF_{75}) \div MEF_{75}$$

$$\frac{MEF_{75} \div PF}{}$$

These three tests are altered by factors that change the instantaneous air flow at any place in the FEFVC between PF and 75% expired VC. They will vary in the same way as the previous 3 tests.

$$MEF_{50} - MEF_{75}$$

$$(MEF_{50} - MEF_{75}) \div MEF_{75}$$

$$\frac{MEF_{50} \div MEF_{75}}{}$$

These three tests are altered by factors that change the instantaneous air flow at any place between 50 and 75% expired VC; presumably by changes in air flow due to obstruction in the small airways. These tests may be helpful in differentiations of obstructive changes more proximal or distal in the small airways if it is true that the  $MEF_{50}$  and the  $MEF_{75}$  reflect air flow limited by more proximal or distal small airways.

## Discussion

This extension of the pulmonary function study done in the Bloomington school system to FEFVC analysis contains two tests,  $MEF_{50}$  and  $MEF_{75}$ , which are simple to do and which can contribute much to the understanding of the contribution of small airway obstruction to air flow in childhood lung disease.

An additional 13 tests are recorded which require careful evaluation before their value for routine use can be established. Although twelve have been presented in four groups of three tests, a search for other ways to compare them may be valuable. For example, if one accepts the real but small error of extrapolating, then  $(PF - MEF_{50}) \div MEF_{50}$  compares the relative deceleration of flow rates during the first and second halves of the vital capacity just as the  $(MEF_{50} - MEF_{75}) \div MEF_{75}$  compares deceleration of flow rates in the 3rd and 4th quarters of the vital capacity.

Whatever the ultimate clinical usefulness of these tests, most of them show changes with height which are almost identical for boys and girls so that little information would be lost if one formula were to be used for both sexes. Even for the tests with the greatest differences between the regression line formulas, the differences at the extremes of height are less than one standard deviation of either variable. Thus, for these extended pulmonary function tests, the sex differences in childhood again appear to be of little significance.

The data from this study should be useful to physicians interested in using FEFVC studies in the care of pediatric pulmonary disease among patients from a similar Caucasian population.

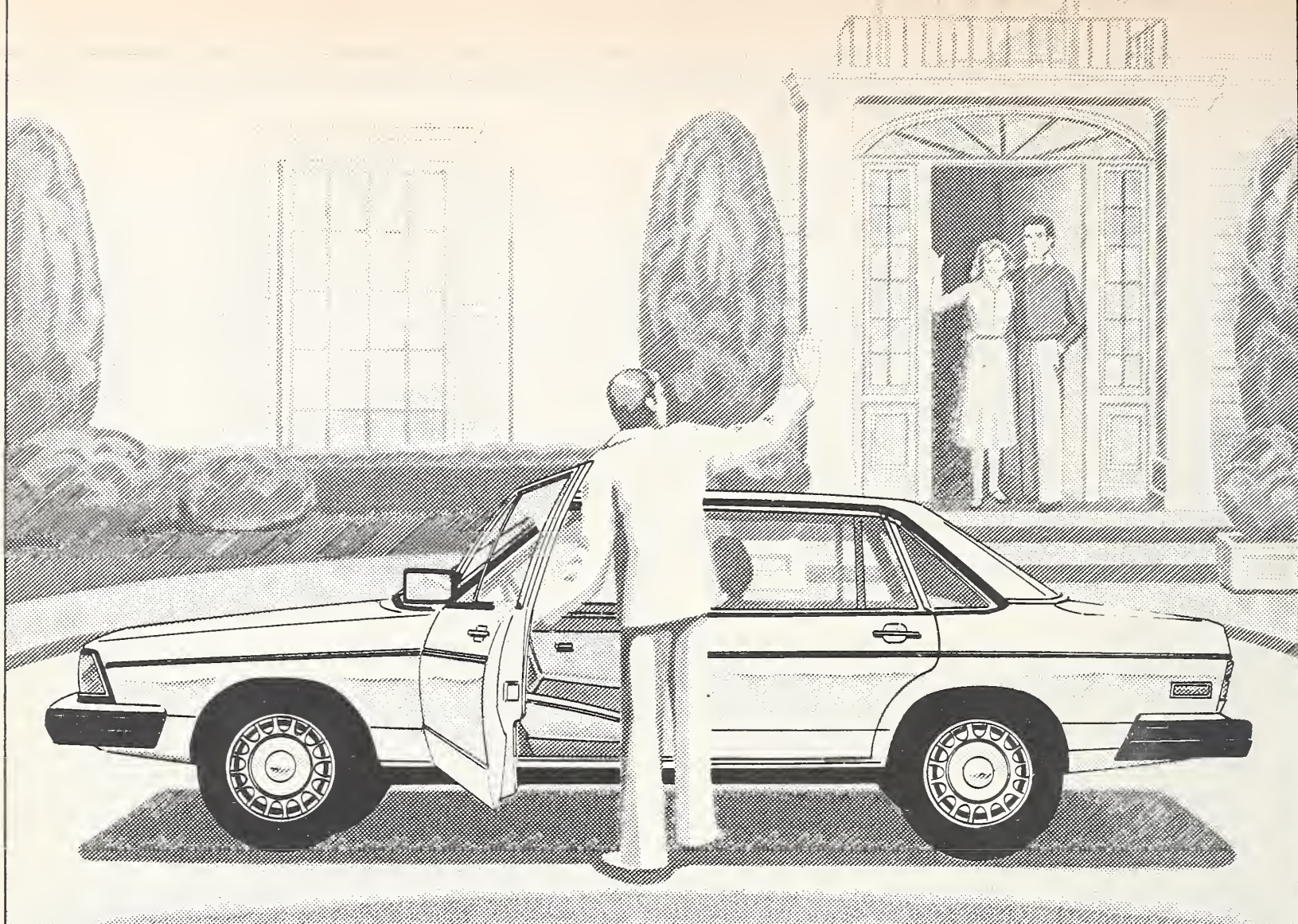
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University of Health Sciences/The Chicago Medical School announces a symposium on "Changing Concepts in Trauma Care" on Saturday, June 7, 1980, at the Marriott Lincolnshire Resort, Lincolnshire, Illinois. A distinguished faculty from leading universities in the country will participate in the symposium. Ample time for pre-and post tests and question and answer sessions has been allotted. Registration fee: Physicians-\$100, residents-in-training, nurses, paramedics-\$50, including a luncheon with the faculty. For further information call Miss Christine Chiaramonte at 312-770-2243 or-2369, or Dr. Sriram at 312-770-2000 or write to Miss Chiaramonte at Saint Mary of Nazareth Hospital, Room 1043, 2233 West Division Street, Chicago, Illinois 60622.





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# Minnesota Medical Association

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#### Thomas G. Briggs, M.D.

Board certified in family practice, Dr. Briggs has served as MMA secretary since 1978. He practices in White Bear Lake and is the medical director of St. John's Hospital Chemical Dependency Unit.

In 1976, Dr. Briggs was president of the Ramsey County Medical Society. He has served on the MMA Subcommittee on Alcoholism and Drug Abuse now called the Resource Group on Alcoholism and other Chemical Dependencies since 1970 and as chairman since 1975. He has also been active on the Legislative Committee, the Public Health Education Committee, the Administration and Finance Committee, and the Membership and Public Services Council.

His past committee activities include General Practice, Family Practice, and Mental Health. Dr. Briggs has also served as a MMA Delegate.

#### Charles J. McCarthy, M.D.

Dr. Charles J. McCarthy is board certified in obstetrics and gynecology and is in private practice in St. Paul.

Dr. McCarthy has served as a MMA Trustee from the 5th District since 1973. He was secretary of MMA from 1969 to 1972. His MMA committee activities include the Administration and Finance Committee and the Perinatal Mortality Subcommittee. Presently, Dr. McCarthy is also a Ramsey County Medical Society Trustee.

He is a member of the Minnesota OB-GYN Society, the Central Association of OB-GYN, the American College of OB-GYN, the American Board of OB-GYN, and the American Society for Calposcopy and Calpo-microscopy.

### 1st Vice-President

#### Dean D. Nywall, M.D.

Dr. Dean Nywall has been in practice in Slayton for 29 years. He has served as MMA Delegate and on the Rural Medical Service Committee.

In 1963, he was president of the Southwestern Minnesota Medical Society.

#### Robert M. Wagner, M.D.

Dr. Robert M. Wagner is board certified in obstetrics and gynecology practicing in Edina.

He is a MMA Delegate and Chairman of the Board of Directors of the Hennepin County Medical Society. He was president of the Hennepin County Medical Society in 1979 and secretary-treasurer from 1976 to 1979.



## STATE OFFICER NOMINEES

### Secretary

#### Richard P. Carroll, M.D.

Dr. Richard P. Carroll is board certified in ophthalmology and practices in St. Paul. He is a MMA Alternate-Delegate.

Currently, Dr. Carroll is chairman of the Membership Committee and serves on the Membership and Public Services Council. He is also a member of the Resource Group on Ophthalmology.

#### Phil C. Roy, Jr., M.D.

Board certified in general surgery, Dr. Roy practices in St. Paul. After serving as a MMA Alternate-Delegate from 1975 to 1977, he became a Delegate in 1978.

Dr. Roy is a member of the American College of Surgeons, the American Board of Surgery, and the St. Paul and Minnesota Surgical Societies.

### Treasurer

#### Paul S. Blake, M.D.

Dr. Paul S. Blake was elected MMA Treasurer in May, 1977 and re-elected in 1978 and 1979. He is chairman of the Administration and Finance Committee of the Board of Trustees and a member of the Membership and Public Service Council. He is also a MMA Delegate.

Board certified in neurosurgery, Dr. Blake practices in Minneapolis.

He is a past president of the Hennepin County Medical Society and he has served on the Permanent Evaluation Committee and the Scholarship and Loans Committee.

### Speaker of the House of Delegates

#### Severin H. Koop, M.D.

Dr. Severin H. Koop is a board certified otolaryngologist practicing in St. Cloud. He has served as Speaker of the House of Delegates since 1978. He served as vice-speaker from 1975 to 1978.

In 1975, he began a term as president of the Minnesota Academy of Ophthalmology and Otolaryngology. He also is a member of the American Academy of Otolaryngology, the Minnesota Academy of Otolaryngology, and the Tri-logical Society.

Dr. Koop is a member of the Awards Committee, the Socio-Economic Council, and the Resource Group on the Conservation of Hearing.

### Vice-Speaker of the House of Delegates

#### Donald R. Jorgensen, M.D.

Dr. Donald R. Jorgensen is board certified in ophthalmology and practices in Willmar.

He is a MMA Delegate and a member of the Resource Group in Ophthalmology. In 1975, Dr. Jorgensen was president of the Mid-Minnesota Medical Society.

Dr. Jorgensen is a member of the American College of Surgeons, the American Academy of Ophthalmology, the Minnesota Academy of Ophthalmology, and the Association for Research in Vision and Ophthalmology.

#### Lawrence M. Poston, M.D.

Board certified in family practice, Dr. Lawrence M. Poston was elected vice-speaker of the House of Delegates in 1978 and subsequently elected in 1979. He practices in Caledonia.

Dr. Poston serves on the Liaison Committee on Health Sciences Education and the Membership and Public Services Council as well as being a MMA Delegate.

He is a member of the American Academy of Family Practice. Dr. Poston has also been active in PSQCM (Southern Minnesota PSRO) and the University of Minnesota Rural Physician Associate Program.



# Evaluation

## Evaluation of a Medical Teaching Conference Long-Term Impact upon Participants\*

BARBARA G. COX, B.S.† and ROBERT L. KEITH, M.S.‡

Although evaluation has gained respectability as a component of medical education conferences, the evaluation methods and instruments used by conference planners are often overly simplistic. Moreover, even a sophisticated evaluation of attitudinal and/or cognitive gains in the participants of a medical teaching conference cannot predict whether these gains will be sustained and whether desired behavioral changes will ensue. On the assumption that the real worth of a medical teaching conference is best measured by its long-term impact upon the participants, we conducted a 7-month post-conference evaluation of a week-long program, the 1975 Laryngectomy Rehabilitation Conference. Participants comprised 35 speech pathologists and 35 laryngectomees; different evaluation instruments were used for each group. The resulting data identified the strengths and weaknesses of the conference and indicated directions for change. The planners of the 1976 Laryngectomy Rehabilitation Conference used these evaluation data to design the format and content of their program.

IN RECENT YEARS, evaluation has gained respectability as an integral component of medical education programs concerned with patient education, professional education, and even health education of the public.<sup>1,6</sup> The language and methods used in evaluation and the rationale linking evaluation to education are not widely appreciated by those in the health professions. Individuals with expertise in education and evaluation may not have the opportunity to work with health professionals who plan educational programs. One reflection of the lack of knowledge about evaluation is seen in the simplistic approach to evaluation used at many medical conferences. The questionnaires given to participants ask such questions as "Was this program worth your time?" and "Did you find the content of the lectures interesting?" Answers to these merely give "happiness indexes."<sup>2</sup>

Most educators agree that any learning activity, to be successful, should result in a long-term change in the behavior or the attitude of the participants.<sup>2,6,7</sup> Hence, questionnaires designed to evaluate a medical conference should include items which measure

whether the objectives of the meeting have been met, and to what extent attitudes and behaviors have changed as a result of the conference.

This paper describes the methods and results of a study of the changes in behavior and attitudes of the participants of a medical teaching conference seven months after the conclusion of the conference.

### Description of the Conference

The teaching conference evaluated in this study was a week-long program entitled, "Laryngectomy Rehabilitation Conference," held at the Mayo Clinic in June, 1975. Participants included 35 speech pathologists, 35 laryngectomees, and 17 spouses of laryngectomees. Criteria for admission to the program were as follows: (1) speech pathologists were required to hold an academic degree in speech pathology and to have either limited or no experience in the speech training of laryngectomees; (2) laryngectomees were required *not* to be proficient alaryngeal speakers and to need additional speech training. These criteria were selected for several reasons. A variety of needed learning experiences could be offered to speech pathologists during the week-long conference, thereby increasing the number of professionals in the field who would be qualified to treat laryngectomees. Also, by undergoing supervised training during part of each day with laryngectomees who had limited speaking proficiency, the speech pathologists could learn in an

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\*Presented at the Cancer Rehabilitation Conference, National Cancer Institute, Bethesda, May 26, 1976. This study was funded by Contract CN 45120 from the National Cancer Institute.



actual clinical setting, rather than work under simulated conditions. Finally, the program would increase the speaking proficiency and contribute to the over-all rehabilitation of a sizable number of laryngectomees.

The week-long program consisted of a variety of didactic and demonstration sessions and clinical training sessions for the laryngectomees and speech pathologists. For each clinical training session, one laryngectomee was paired off with one speech pathologist for 1½ hours. The eight speech pathologists from the faculty who supervised these 35 pairs throughout the week were specialists in teaching alaryngeal speech. The 17 spouses who attended the conference were invited to participate in any of the didactic or clinical sessions they wished.

Several objectives were set for the two participant groups. For speech pathologists, the primary objectives were to learn the training methods for esophageal speech, to become acquainted with the various

mechanical devices now available for alaryngeal speech, and to become familiar with the supportive needs of the laryngectomee and his or her spouse. For laryngectomees, the primary objectives were to become more proficient in alaryngeal speech during the one-week training period, to acquire the knowledge and skills necessary to continue learning at home, to be referred to resources in their home areas for continued training and/or support, and to acquire insights into sharing adjustment problems with their spouses.

At the end of the program, the registry examination sponsored by the International Association of Laryngectomees was administered to those speech pathologists who wished to take it.

At the close of the conference, a simple evaluation form was distributed to attendees for them to complete and return by mail. Seven months later, more-detailed evaluation instruments were sent to the participants. One form was designed for speech pathologists and one for laryngectomees. The purpose of these

**TABLE 1**  
**Speech Pathologists Seven Months Post-Conference: Subjective Assessment of Long-Term Professional Improvement and Responses to Conference**

	Responses (31 Speech Pathologists)					
	<i>Def. True</i>	<i>Mostly True</i>	<i>Don't Know</i>	<i>Mostly False</i>	<i>Def. False</i>	<i>Not Answered</i>
1. I feel much more comfortable working with laryngectomees now than I did before the conference.	25	4	1	—	—	1
2. My ability to treat laryngectomees has improved significantly as a result of the conference.	21	8	1	—	—	1
3. I learned more from the supervised patient-therapist confrontations than I did from the talks.	4	3	9	13	2	—
4. I wish it had been suggested that I bring along a tape recorder and/or other materials that I customarily use during therapy.	6	11	5	5	1	3
5. I would have benefited from a suggested reading list sent out in advance of the conference.	9	15	5	—	—	2
6. I would have liked "hand-outs" or reprints at the conference, relating to the subjects discussed.	23	5	2	—	1	—
7. I would have liked a selected bibliography to take home.	23	4	1	1	—	2
8. Small group discussions with laryngectomees and their spouses would have been a good addition to the program.	18	5	6	2	—	—
9. Sessions should have been planned just for the spouses of laryngectomees.	12	13	5	1	—	—
10. I would have liked more personal interaction with the staff.	7	12	6	3	2	1



instruments was to determine whether the enthusiasm and motivation reflected in the immediate post-conference surveys were sustained, and whether behaviors and/or attitudes had been altered in accordance with the conference objectives over an extended period of time.

### Evaluation Methods and Instruments

The evaluation instruments sent to speech pathologists and laryngectomees 7 months after the conference were divided into three parts. The questionnaire sent to the speech pathologists included: (1) subjective measures of professional improvement since the conference and sustained reactions to the program, (2) objective measures of professional behavioral and attitudinal changes, and (3) open-ended questions on how the next program could be improved. The questionnaire sent to the laryngectomees included: (1) subjective measures of speech improvement and spouses' reactions to the program, (2) objective measures of health-behavioral change, and (3) open-ended questions on how the next program could be improved.

### Evaluation Results

Of the 35 speech pathologists who were sent evaluation forms, 31 responded (87%). Of the 27 laryngectomees who could be contacted, 24 responded (89%). Every evaluation form was filled in thoroughly, and numerous unsolicited comments were added.

#### *Evaluation Data Received from Speech Pathologists.*

The subjective responses from Part 1 of the survey (Table 1) indicated that 29 of 31 speech pathologists who responded felt more comfortable working with laryngectomees and that their ability to treat laryngectomees had improved considerably during the 7-month interval since the conference. A number of suggestions for improving the next conference were made, including requests for tape recorders and other materials that speech pathologists customarily use during therapy (55%), hand-outs or reprints to be distributed at the conference (91%), small-group discussions with laryngectomees and their spouses (75%), and special sessions for the spouses (81%). Other respondents stated that the clinical sessions balanced well with the didactic sessions, and that one-to-one interactions between the staff and the speech pathologists were of high quality.

Objective measures of change in the professional skills and experiences of the speech pathologists are shown in Table 2. Of the nine speech pathologists who

had treated no laryngectomees before the conference, four had begun working with them in the 7-month interval after the conference. Of the 22 who treated laryngectomees before, eight (26%) experienced an increased caseload. Before the conference, only 18 of the 31 respondents (58%) understood the three methods of air intake used by alaryngeal speakers; at 7-month post-conference evaluation, 30 of the 31 understood these methods. Only nine of the speech pathologists could produce esophageal sound themselves at the time of the conference; 7 months later, an additional seven stated that they could accomplish this.

The open-ended questions regarding the content and format of the conference elicited many detailed and varied responses. Answers to the first question, "What parts of the Laryngectomee Rehabilitation Conference had the greatest lasting impact on you?" reflected the respondents' sustained enthusiasm toward almost all aspects of the conference. The opportunity to work with laryngectomees under clinical supervision and the interaction with the teaching staff were frequently mentioned. There were favorable comments on the benefit gained from the variety of theoretical and practical information and from the multidisciplinary composition of the teaching staff.

To the question, "What subjects do you think

**TABLE 2**  
**Speech Pathologists Seven Months Post-Conference:**  
**Objective Measures of Professional**  
**Improvement Resulting from Conference**

	Responses (31 Speech Pathologists)		
	Yes	No	Not Answered
1. Did you treat laryngectomees before coming to this conference?	22	9	—
2. If no, do you treat them now?	4	5	—
If yes, do you treat more than you used to?	8	13	1
3. Did you understand the three methods of air intake before coming to the conference?	17	13	1
If no, do you understand them now?	12	1	—
Can you teach all three methods?	24	5	2
4. Did you take the I.A.L. registry examination at the conference?	22	9	—
If no, do you plan to take it?	5	4	—
If yes, did you pass?	20	2	—
5. Were you able to produce esophageal speech yourself before the conference?	9	22	—
If no, can you do it now?	7	15	—



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should be added when the conference is given again?'' most responses fell into two categories. The speech pathologists wanted more information and guidance on counseling the patient and spouse, helping the patient cope with the emotional aspects of his or her condition, and integrating knowledge of the psychosocial impact of laryngectomy into the therapeutic setting. The speech pathologists also wanted more detailed coverage of the clinical techniques for teaching esophageal speech, especially the advanced aspects.

The general suggestions made by speech pathologists for improving the conference showed a

need for more clinical supervision and feedback from the faculty during the clinical training sessions with the laryngectomees. They also suggested a reduction in lectures given by health professionals in areas not directly related to speech therapy, so that more time could be devoted to the supervised clinical sessions.

#### *Evaluation Data Received from Laryngectomees.*

According to the subjective responses from laryngectomees (Table 3), 23 of the 24 respondents (97%) felt that their confidence had improved as a result of the conference. Twenty respondents (83%)

**TABLE 3**  
**Laryngectomees Seven Months Post-Conference:**  
**Subjective Assessment of Long-Term**  
**Health-Behavioral Improvement and Responses to Conference**

	Responses (24 Laryngectomees)					
	<i>Def. True</i>	<i>Mostly True</i>	<i>Don't Know</i>	<i>Mostly False</i>	<i>Def. False</i>	<i>Not Answered</i>
1. My confidence in my ability to improve my speech rose as a result of the conference.	19	4	1	—	—	—
2. My speech has improved since the conference.	16	4	3	—	—	1
3. I would have liked more demonstrations on the first steps in learning esophageal speech.	13	5	3	1	2	—
4. The laryngectomee speakers at the conference gave me more confidence because they offered proof that "it can be done".	22	2	—	—	—	—
5. The films showing laryngectomees using esophageal speech were useful and encouraging.	16	6	2	—	—	—
6. I had plenty of time at the conference to have all my questions answered.	13	9	—	1	—	1
7. Enough time was devoted to discussion of the adjustment problems of the laryngectomee's family after surgery.	5	9	3	4	1	2
8. Less time should have been devoted to the causes of cancer of the larynx and surgery.	3	5	4	6	4	2
9. More time should have been devoted to informal group discussions.	13	3	5	2	—	1
Note: The following statements are only for laryngectomees accompanied by spouses (17 laryngectomees)						
10. My spouse learned new, helpful information about my condition at the conference.	14	3	—	—	—	—
11. My spouse and I have expressed our feelings about my condition more openly since the conference.	14	2	1	—	—	—
12. My spouse would have liked more time devoted to the adjustment problems of the husband or wife of a laryngectomee.	9	3	1	3	1	—



stated that their speech had definitely improved. All respondents were enthusiastic about the talks given by invited laryngectomy speakers and most found films of laryngectomees useful. The respondents wanted more demonstrations on the first steps in learning esophageal speech and more informal group discussions. The laryngectomees who were accompanied by their spouses felt that the spouse had learned new, helpful information about the laryngectomy's condition at the conference, and most found that it became easier to express their personal feelings.

Objective measures of health-behavioral changes in the seven-month post-conference interval, shown in Table 4, indicated that 55% of the laryngectomees had changed to a different, more satisfactory method of speaking since the conference. Half of the laryngectomees had been referred to a community resource as a result of the conference, such as a speech pathologist or Lost Chord Club. Twenty-two laryngectomees (92%) reported that they learned at the conference that they had incorrect speech habits; all 22 stated that they improved as a result of what they learned.

Answers to the open-ended questions showed sustained enthusiasm for the conference among the laryngectomees. Half the respondents specifically commented on the individual therapy sessions as having the greatest lasting impact. Suggested subjects to be added to the next conference included laryngectomy expectations throughout the rehabilitation period, steps in learning alaryngeal speech, and adjustment problems of the laryngectomy's spouse and family.

### Discussion

While immediate post-conference evaluations can elicit attitudinal changes and/or cognitive gains in the participants, these may not be sustained over a long period, and such evaluations cannot measure long-term behavioral changes. Presumably, the worth of a medical conference must include some measure of long-term impact upon the participants.<sup>8,9</sup>

On this premise, a seven-month post-conference evaluation was conducted to measure both behavioral and attitudinal changes in two participant groups of a medical conference: speech pathologists and laryngectomees. The questionnaires included a request for suggestions for improving succeeding conferences. The evaluations identified weak areas in content and format, strong areas, and new areas for future development.

One purpose of evaluation is to provide useful data for improving an educational process, and thereby, its

results. Accordingly, the 7-month post-conference data collected from participants in the 1975 Laryngectomy Rehabilitation Conference were used to make appropriate modifications in the next year's conference. Some lectures not directly related to speech therapy were supplanted by clinical training sessions. Speech pathologists were advised to bring tape recorders and other treatment supplies, background literature was made available to them, small-group therapy sessions were added, and more time was devoted to the psychosocial impact of laryngectomy surgery. The laryngectomees were given more opportunity for group discussion, more information about self-care and other aspects of long-term rehabilitation, and guidelines for using and/or developing community resources for laryngectomees. The adjustment problems of the laryngectomy received special emphasis, with one session devoted exclusively to spouses. Through films, demonstrations, and increased clinical training sessions, the laryngectomees received more specific instructions on the steps in learning alaryngeal speech.

The evaluation methods described in this paper can be applied to any medical conference. As a first step, conference planners must establish their objectives, that is, the cognitive, behavioral, and attitudinal changes that comprise the expected outcomes of the conference; this must include important long-term

**TABLE 4**  
**Laryngectomees Seven Months Post-Conference:**  
**Objective Measures**  
**of Health-Behavioral Improvement**  
**Resulting from Conference**

	Responses (24 Laryngectomees)		
	Yes	No	Not Answered
1. Have you changed your method of speaking since the conference? If yes, what method were you using previously? What method are you using now?	13	10	1
	(Comments summarized in Results) (Varied descriptions given)		
2. Were you referred to a speech pathologist or other resource near your home during the conference? What was the resource and how did you benefit, if at all?	12	10	2
	(Comments summarized in Results)		
3. Did you learn at the conference that you had incorrect speech habits?	22	1	1
4. If yes, have you improved as a result of what you learned during the conference?	22	0	2



changes in the professional performance of the conference participants as a result of the educational experience. After all, the worth of a medical educational experience should be measured in terms of improved professional performance.<sup>10</sup> The next step is to incorporate these objectives into the plan for the

content and format of the conference. A final step, after an interval of several months, may then include an evaluation to determine how well the conference met its objectives. The information provided will then afford those responsible for planning another session the opportunity to improve the educational program.

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# Rheumatology Corner

## Carpal Tunnel Syndrome

ERIC SIGMOND, M.D.\* and H.S. LUTHRA, M.D.†

OF ALL THE various neuropathies seen in rheumatic diseases, entrapment neuropathies are most common and among these carpal tunnel syndrome is the commonest. Entrapment of the median nerve by swelling from synovitis or other damage to the wrist joint can lead to this complication. The carpal tunnel is bounded by the carpal bones and the transverse carpal ligament (flexor retinaculum). Through this tunnel pass the flexor tendons of the hand along with the synovial sheaths covering them. The median nerve passes superficial to these tendons but deeper to the thick fibrous flexor retinaculum. In view of the nerve being surrounded by tight structures, swelling from collection of fluid, synovitis, scarring, disorganization of the joints with or without dislocation of the bones can cause impingement of the nerve and give rise to symptoms. Although among the rheumatic diseases, rheumatoid arthritis is the most common cause of the carpal tunnel syndrome. Other conditions can also give rise to it. These conditions are listed on the Table.

Patients usually complain of paresthesias along the distribution of the median nerve which supplies the skin over the first three fingers and the lateral half of the fourth finger on the palmar aspect. The median nerve, after it passes through the carpal tunnel also sends out a branch which supplies the thenar muscles. The earliest symptoms may occur at night with severe paresthesias or pain. Gentle massage and wringing of the hands usually results in relief of the symptoms in a few minutes. Symptoms can also occur from use and patients complain of symptoms occurring while knitting, sewing, holding a book, reading the newspaper, writing, etc. Occasionally, the impingement may be quite severe and the patients may be symptomatic all the time.

On examination there may be no positive findings, but certain maneuvers like hyperflexion of the wrist joint (Phalen's sign) and percussion of the median nerve over the carpal tunnel (Tinel's sign) would reproduce the paresthesias. In patients who have

TABLE 1

### Conditions associated with Carpal Tunnel Syndrome.

#### A. Systemic disease:

1. Rheumatoid arthritis
2. Systemic lupus erythematosus
3. Myxedema
4. Acromegaly
5. Diabetes
6. Amyloidosis

#### B. Trauma, leading to:

1. Hematoma
2. Dislocation and/or fracture of the carpal bones

#### C. Miscellaneous

1. Ganglion cyst
2. Deposits of mono sodium urate or calcium pyrophosphate dihydrate crystals
3. Osteophytes
4. Nonspecific tenosynovitis
5. Pregnancy

muscular involvement there may be obvious atrophy of the thenar muscles as well as weakness of the opponens pollicis and abductor pollicis brevis.

The diagnosis is made mainly by history and examination. If, however, there is some doubt, especially in patients complaining of retrograde paresthesias to the elbow or even shoulder, one should try to differentiate from a root lesion with electromyography (EMG). EMG changes of the thenar muscles and conduction delay of the median nerve at the carpal tunnel are diagnostic. Rarely the patients may have a negative EMG even though they are symptomatic.

Treatment initially should be conservative. Reassuring the patient as well as using local measures such as splinting of the wrist, especially at night may be adequate. If the symptoms persist, then injection of local anesthetic with insoluble steroids may give relief. Failure of conservative treatment, severe pain, presence of symptoms for long duration, EMG evidence of progressive compression, and thenar muscle atrophy would be indications for surgical intervention. Surgical results are generally very good.

\*Current address: Northbrook, Illinois.

†Mayo Medical School, Rochester, Minnesota



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# Minnesota Medical Association

## 1980 MMA Annual Meeting

The 1980 MMA Annual Meeting is planned to be informative, productive, and efficient for all physicians who attend. This year's annual meeting will be held on Tuesday, Wednesday and Thursday — May 20, 21 and 22 at the Radisson South Hotel in Bloomington. This is contrary to past annual meetings which have been held on Wednesday, Thursday, and Friday.

On Tuesday, May 20, reference committees will meet in the afternoon, followed by the opening of the House of Delegates. Reference committees will convene again in the evening. During the day golf and tennis activities are planned.

The Scientific Assembly Program will begin on Wednesday morning, May 21. The Annual Meeting luncheon will be held at noon featuring an important speaker. After the luncheon, the scientific assembly will resume. The Awards Banquet, which has always been a highlight of every Annual Meeting, will take place Wednesday evening.

Thursday, May 22, will bring more scientific program offerings in the morning. The House of Delegates will convene for its closing session in the afternoon.

Several interesting and vital issues will come before the 1980 House of Delegates: the proposed revision of the AMA Code of Ethics has caused discussion and thought all over the nation;\* the MMA study of the formation of a physician owned professional liability insurance company; redistricting of the MMA Trustee districts, and election of MMA Trustees Officers.

The Scientific Program is once again being developed with an eye for the contemporary needs of the practicing physician. Examples of courses which will be offered at the 1980 Annual Meeting are: Update in Clinical Virology; Socio-Economics of the Health Care Delivery System; Disease and Cultural Problems of the Indochinese Refugees; Risk Management; Selected Tools of Preventive Medicine. A full program of course offerings will be published in the near future.

\*See page 183.

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75 MINUTES FROM Minneapolis. Group of four Family Physicians wants to add a surgeon and another Family Physician. Beautiful city with lakes + parks. Incorporated group which stresses family life and free time. HEW designated physician shortage area. Minnesota Medicine, (548) 101 E. 5th St., #900, St. Paul, MN, 55101.

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## President's Letter

This year, in the week of 19 May, your elected representatives will gather at the Radisson Hotel in Bloomington for the Annual House of Delegates meeting of the MMA. This meeting will, again, be a living demonstration of the democratic process in its purest form. It is pure because those who have a vote are duly elected from the constituency which they represent, and none of those who participate in the process are motivated by personal gain. Neither the delegates nor the officers are salaried. In fact, I believe, it is accurate to state that because of time given to the Association, many of those involved may suffer loss of personal income. Finally, the agenda items, this year, as in previous years, will almost without exception deal with problems relating to the health and care of individual patients. Nowhere in that meeting will one hear of how the system might be made more profitable for physicians. Instead, we will hear discussion about the best method of assuring quality, confidentiality, cost effectiveness, and maintenance of human freedom with personal liberty.

No one who has attended a session of the meeting of the House of Delegates of the MMA can fail to be impressed. Indeed, I would be surprised if such exposure did not arouse a keen desire to be involved and become part of this process which is basic to the health of our country. Our Association, as an example of the democratic process, must continue to strengthen itself and refine its structure to become ever more representative and responsive. It is essential in this regard that all eligible persons be members of the Association, and of those, as many as possible should be actively involved.

In the hope that exposure will be followed by commitment, the MMA has established a policy which permits a member physician to bring a non-member physician as a guest to the annual meeting. The understanding is that the guest physician would not be required to pay the usual registration fee. In exchange for this courtesy, the host physician would assume responsibility for exposing his guest to the deliberations of the House of Delegates and to the work of the reference committees. The name and address of the guest would, of course, be registered and he/she could expect a follow-up contact from our membership committee.

I encourage each of you to attend this annual meeting and give serious thought to bringing, as your guest, a student, resident, or practicing physician who is not yet a member of the Association. If enough of us take advantage of this opportunity, the meeting in 1980 could be the most interesting, exciting, and profitable ever. I look forward to greeting each of you at that meeting.

Frank E. Johnson, M.D.  
President  
Minnesota Medical Association

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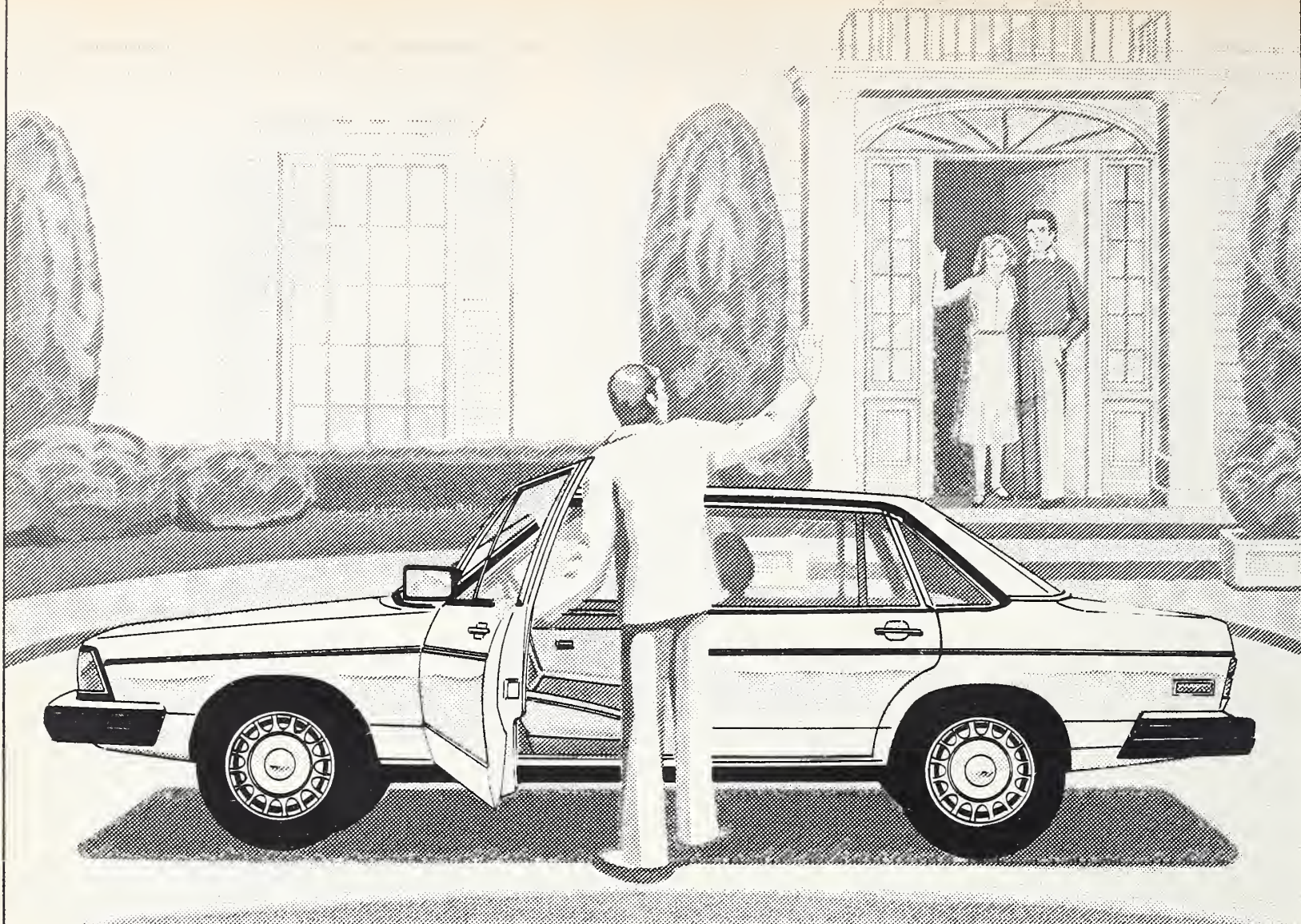


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## Editor's Notebook

### Responses to HMO Editorial

Responses to my February 1980 HMO editorial have been varied and vigorous. They have come from fee-for-service physicians, hospital administrators, AMA officials, HMO physicians, and HMO advocates. The number of responses surprised and impressed me. People, it appears, feel deeply about HMOs. I shall now comment on the responses I received.

#### Fee-for-Service Physicians

To the man, fee-for-service physicians praised the editorial's sentiments and tone. If you'll recall, I said rapid local HMO growth ought to be put in a national perspective. By the end of 1979, 16 percent of Twin Citians belonged to HMOs, but nationally the figure was closer to four percent. There are three ways to explain this discrepancy: (1) the Twin Cities are innovative, progressive, and ahead of the rest of the country; (2) the Twin Cities have special circumstances, e.g. a collectivist social philosophy, that does not exist elsewhere; or (3) a combination of these factors have put us in the forefront of the HMO and health care cost reduction movement. Anyway, for unclear reasons, HMO membership is doubling every three years in the Twin Cities, but has yet to take off nationally, at least not enough to be a competitive force in most regions.

Among responses from fee-for-service physicians were these: "That was the clearest exposition of HMOs I have read." "It's about time we had a little counter propaganda on HMOs." "Nicely balanced." "I'm glad someone has finally put HMOs in perspective." "You're dead right." Many who spoke out were young physicians who were establishing practices. They were feeling HMO competition heat and thought HMOs had unfair marketing advantages. Signing up of large blocks of patients before the patients have ever been exposed to the fee-for-service physician disturbed them.

I could not help but observe that recently the Physicians' Health Plan has launched a radio advertising campaign to attract patients. This campaign no doubt was partly to counter similar Group Health radio advertising. In any event, as HMO proponents have predicted, HMOs have brought competitive health care to the Twin Cities.

#### Hospital Administrators

Hospital administrators, as you might expect, were decidedly neutral. This figures. After all, HMO patients represent a sizable group of patients. Yet fee-for-service patients still make up the bulk of hospital patients. Administrators are sharply aware the essential HMO strategy is to keep patients out of hospitals. But with a shrinking hospital population, wise administrators cultivate all potential clients.

#### Organized Medicine

One AMA official asked for a passel of reprints to distribute to other AMA officials. Another reader, an AMA delegate, wanted to share copies with Congressmen and Senators. From AMA people and from physicians, I have learned the whole country has its eye on the Minnesota HMO experience. Indeed, many Minnesota physicians are sending copies to friends in other states to inform them of what's happening here.



### HMO Physicians

HMO and ex-HMO physicians were dispassionate about the editorial. To them, working for an HMO or setting up a private practice involves trade-offs. HMOs offer a high starting salary, liberal fringe benefits, no overhead, few management problems, shorter working hours, time to enjoy family and personal life, and security. On the other hand, HMOs have problems too: no practice outside the confines of the HMO, a limitation to the procedures one can order, in rules about who to hospitalize, a relatively fixed salary and no equity. HMO physicians informed me they didn't foresee further HMO growth in the Twin Cities. More HMOs would spoil the pre-paid broth. Also I learned one Minnesota HMO, Group Health of Northeastern Minnesota, has experienced problems staying in existence.

### Ellwood Letter

One letter in particular brought my editorial into sharp focus. The letter was from Paul Ellwood, Jr., M.D. Doctor Ellwood, as you may know, is credited with launching the HMO movement and with selling the concept to Congress and the Nixon Administration in the early 1970s. For at least ten years, and probably more, he has persistently, staunchly, and eloquently presented the case for letting competitive market forces hold down health care costs. He is proud of the vitality and force of HMO growth in the Twin Cities. Presently, he is President of Interstudy, an Excelsior-based health care consulting firm. This firm wields considerable influence in public and private health care decision making.

Doctor Ellwood's letter follows:

"I was really rather surprised and disappointed at the negative tone and reliance on innuendo in your February 1980 Editor's Notebook. Since we have something going on locally in health care that has attracted the admiration of the rest of the country, what can be gained by constructing a series of arguments that what we've done can't be achieved anywhere else? It seems to me that you've provided beautiful ammunition for further stonewalling any innovation in medical care among communities whose health systems lag far behind ours in both fee-for-service and prepaid medical care.

Furthermore, the data on which you relied was out-of-date. HMOs here and elsewhere in the country are growing at a remarkable rate. Your implication that their growth is slowing down here is contrary to the latest information we have which shows a continued 30% annual growth rate in the Twin Cities (12/78 to 12/79). Nationally, enrollment increased by 20% in 1979 to an estimated 8.9 million people.

Your characterization of the Twin Cities as a 'hot bed' of billion dollar corporations, in which you compared the number of billion dollar corporations in Minneapolis/St. Paul to entire states, was a beautiful example of how to manipulate statistics. Instead of using the population of Minneapolis/St. Paul as the denominator for the concentration of billion dollar corporations in the state, why didn't you use the entire state's population? Or if you would like to find a community where there is a real concentration of billion dollar corporations, look at Stamford, Connecticut, which I believe has 25 Fortune 500 corporations concentrated in a community that isn't nearly as large as the Twin Cities.

There are plenty of thoughtfully critical things that can be written and explored about the rapid changes that are taking place in our community's health system, but I was sorry to find few of them in your recent editorial."



### Response to Response

My editorial and Doctor Ellwood's response illustrate two old truths: (1) where you stand depends on where you sit; and (2) you can use the same statistics to support different positions.

As the Editor of a state medical journal, addressed primarily to fee-for-service practitioners, I argue in my editorial that a government-sponsored movement that has enrolled only 7.4 million of 222 million Americans can hardly be considered the wave of the future.

As the leading spokesman for the HMO movement, Doctor Ellwood counters by noting that I used dated enrollment figures, that the yearly United States HMO figures increased from 7.4 to 8.9 million from 1978 to 1979 (a 20 percent increase), and that the Twin Cities HMO membership went up 30 percent in the same year.

If I were an arguing man, I would say that 8.9 million still only represents 4.0 percent of all Americans. Of course, if you extrapolated a 20 percent annual increase out 10 years, you would have about 48 million Americans in HMOs by 1990. But that's Ellwood's argument, not mine. Besides, arguments about the future are difficult because they involve the future.

### The "Right Mix"

In my editorial, I put forth the proposition that Twin Cities HMO growth rests on the "right mix" of local ingredients. This mix, I speculated, included: (1) a tradition of group practice; (2) a large number of medical school graduates with resulting surplus of physicians; (3) a progressive collectivist political tradition; (4) a high proportion of citizens with hospital insurance; (5) a low proportion of minorities; (6) a well-educated populace knowledgeable in health care matters; (7) the existence of three or more established competitive plans; (8) a sophisticated marketing environment; (9) the presence of articulate HMO spokesmen; (10) an open-minded medical profession; and (11) a heavy concentration of major corporations.

Ellwood picks me up here by saying that: (1) I'm "constructing a series of arguments" that show "what we've done can't be achieved elsewhere"; and (2) I'm comparing apples to oranges, i.e. the concentration of corporations in cities of Minneapolis-St. Paul to entire states. He points to Stamford, Connecticut, as an example of a city with a really heavy concentration of major corporations. HMOs have not taken root there.

### Minnesota and Connecticut

As a physician who came to Minnesota from Connecticut, I can attest to a different "mix" in Connecticut, a state that has about one-fifth the number of HMO participants per capita as Minnesota. Connecticut, for example, has almost no tradition of group practice, is more conservative politically (no state income tax), has a higher proportion of minority groups, has a much greater ethnic heterogeneity, has few experienced HMO spokesmen in the medical community, and has only one HMO with a track record of more than five years. Now, five HMOs or IPAs (Independent Practice Associations) exist within Connecticut, but one is presently in receivership. Hartford, the hub of a metropolitan region of about one million, has only one fledgling HMO. There's a serious question whether it will survive. Further, Connecticut physicians and health officials are now skittish about setting up more HMOs following the national publicity after a Fort Collins, Colorado, HMO collapsed.

As Doctor Ellwood observed, the part of the "mix" that Connecticut shares with Minnesota is the heavy concentration of billion dollar corporations. Indeed, if you recalculate the concentration of these corporations using the populations of the states as a whole, Connecticut has 9.3 major corporations per million citizens, while Minnesota has 6.3 corporations per million citizens. But there is a difference between the two states'



corporations. Most Connecticut corporations have migrated to Stamford from New York City in the last 10 to 15 years, while the Minnesota corporations are "home-grown", i.e. originated in Minnesota. This fact gives the Minnesota corporations more civic clout and more familiarity with the local medical environment. In Connecticut, many of the major "home-grown" corporations are insurance companies — Aetna, Travelers, and Connecticut General. These companies, my physician friends in Connecticut tell me, are at best luke-warm about HMO development within Connecticut.

I don't wish to overwork the Minnesota-Connecticut analogy. But it illustrates that regional differences play a powerful role in promoting or inhibiting HMO growth. The sheer momentum of the national HMO movement may smooth out or erase these regional differences. I, for one, remain skeptical that this will happen voluntarily.



**Cover Painting**

"Through the Wood"

"Through the Wood" is a Nikon photograph Dr. Frances Elizabeth Schaar took of one of her oil paintings made while a student of the French Impressionist Alma Trulis of Minneapolis. Dr. Schaar is active in two local camera clubs. She is a pediatrician who practiced many years in Minneapolis. Currently she is a part-time instructor in continuing education courses for nurses at two of the Community Colleges.

She belongs to the Minneapolis Color Photo Club in addition to two other photography clubs. She has had three covers on MINNESOTA MEDICINE: February 1966, January 1973, and October 1977.

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# Candidacy



Robert T. Kelly, M.D.

Dr. Robert T. Kelly, after a long career in medical affairs in the Range County Medical Society, the Minnesota Medical Association, and the AMA, is a candidate for the Board of Trustees of AMA.

Bob has served as an AMA Alternate Delegate and Delegate for twelve years in the House and chaired the MMA delegation. He was elected to the Council on Medical Service in 1974 and was recognized there for his leadership by being elected successively Vice-Chairman and Chairman of that Council. He headed an ad hoc committee on PSRO of the Council. He is a member of the National PSRO Advisory Council; served on the AMA Speaker's Bureau; and chaired the Ad Hoc Committee on Practice Evaluation.



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# Hypercalcemia in Chronic Myelogenous Leukemia

DANIEL T. GROEBNER, M.D.;\* JOHN N. MORK, M.D.† and JOHN F. BARLOW, M.D.†

Measurement of parathyroid hormone (PTH) in a case of hypercalcemia associated with chronic myelogenous leukemia (CML) is reported. This case is consistent with ectopic production of PTH. Clinical and pathological characteristics of hypercalcemia in CML are reviewed. Hypercalcemia developing in the course of CML may be a marker of early blastic transformation.

**H**YPERCALCEMIA IS an uncommon complication of leukemia, with grave prognostic implications. The cause of hypercalcemia in leukemia is not known. Recent availability of a satisfactory assay for parathyroid hormone (PTH) has improved our understanding of this unusual form of hypercalcemia. We present a case of hypercalcemia in the course of chronic myelogenous leukemia (CML) with evidence for ectopic hyperparathyroidism.

## Case Report

A 42 year old woman, was admitted to Worthington Regional Hospital, February 18, 1977, for evaluation of weakness, weight loss and cough.

Chronic myelogenous leukemia was diagnosed in June 1972 during an evaluation of menorrhagia. A single course of busulfan (154 mg over a period of 18 days) induced a remission that lasted 4½ years. Bone marrow examination in June 1976 suggested early relapse with myeloid predominance, with increased numbers of promyelocytes and myelocytes. Because of increasing WBC and platelet count (respectively 54,000/mm<sup>3</sup> and 775,000/mm<sup>3</sup>) she was given a second course of busulfan starting on 12/30/76. This course lasted 14 days and totalled 84 mg. of busulfan. Remission in the peripheral blood was incomplete with a decline in WBC to 7700/mm<sup>3</sup> but a decline in platelet count to only 480,000/mm<sup>3</sup>. The second remission lasted only a month.

During the first remission of four and a half years she experienced recurrent oral and genital herpes. Dysfunctional uterine bleeding that lead to a hysterectomy. *M. Kansasii* pneumonia that required a diagnostic thoracotomy. She required separate courses of prednisone for (1) subacute thyroiditis (2) maculopapular rash, and (3) drug reaction to rifampin (manifest by fever, hemorrhage, thrombocytopenia, leukopenia and erythema nodosum).

During the second remission from the CML anorexia, cough and weight lost appeared and led to her admission on 2/18/77.

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## Physical Examination

Height 162.5 cms, weight 57.5 kgs, temperature 37 C., pulse 88 and regular and respirations 16/min. The lungs were clear to auscultation. An S4 heart sound was heard. There was tenderness of the medial aspect of the left knee. Induration of the upper lip was thought to be caused by a recent herpes simplex infection. There was no enlargement of spleen or lymph nodes.

## Laboratory Data

On admission the hemoglobin was 10.6 gm%, hematocrit 33%, WBC 22,300/mm<sup>3</sup> with 63% PMNs, 26% lymphocytes, 3% eosinophils, 5% band forms, 3% metamyelocytes. Platelets were 602,000/mm<sup>3</sup> and erythrocyte sedimentation rate 74 mm/hour. Calcium was 11.2 mg%. Prothrombin time, partial thromboplastin time and fibrinogen were all normal. A bone marrow biopsy on 2/22/77 showed a markedly hypercellular marrow with focal myelofibrosis and collections of immature cells. Admission creatinine was 1.3 mg%, BUN 19 mg%. On 2/23/77 PTH in serum was

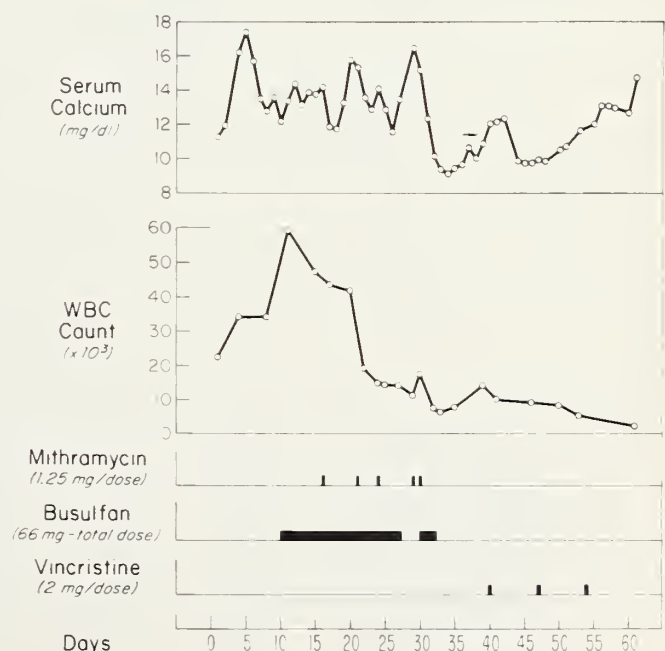


Figure — Graphic representation of serum calcium in relation to the white blood cell count and three selected treatment modalities.



30 ul Eq/ml (by RIA at Mayo Clinic laboratories where normal is 0-40 ul Eq/ml.)

#### Hospital Course

The patient became weaker and mentally more sluggish during the first three hospital days. Because of initial serum calcium elevation, serial determinations were obtained (Figure). Treatment for the hypercalcemia was started with saline infusion, furosemide, intravenous hydrocortisone and a balanced phosphate solution intravenously and orally. During the next week the above measures were successful but, frequent repetition of oral or intravenous phosphate was required in order to maintain a serum calcium below 14 mg%. Mithramycin was started and continued intermittently with improved control of serum calcium. Eventually low platelet counts precluded further treatment with mithramycin. Vincristine was added, 2 mg IV each week, and prednisone was increased from 40 mg to 60 mg per day. The serum calcium responded well with a decline to normal levels. In spite of this she continued to deteriorate clinically.

Other problems contributed to her eventual demise. She had progressive renal failure with a creatinine of 4.0 mg%. Anemia was another recurrent problem with frequent transfusions required. A right axillary lymph node became prominent, and a needle biopsy showed diffuse infiltration with immature cells. She had a chronic cough

which could not be suppressed by codeine or other medications. Bone pain was incessant and required narcotics. She was bedridden and terribly wasted, her weight falling to 53 kgs. Shortly before death, chest Xray showed a new rib fracture with callus formation, multiple tiny lytic lesions of the ribs and left humerus and bilateral pleural effusion. A thoracentesis was nondiagnostic. Attempts to treat a presumed recurrence of *M. Kansasii* pneumonia were unsuccessful. She expired April 20, 1977.

Autopsy findings included focal blastic transformation of the bone marrow as well as leukemic infiltrate in the spleen and kidneys. The lungs were the site of diffuse interstitial pulmonary fibrosis as well as massive calcification. Focal calcifications within the heart were accompanied by focal myocardial necrosis. Three parathyroid glands were definitely identified. The glands were not enlarged and showed a normal amount of fat. Hyperplasia or adenoma was not identified within the parathyroid glands. Although only three parathyroid glands were found, a careful search was conducted and no adenoma was seen in the usual locations or in the paraesophageal region or mediastinum.

#### Discussion

Hypercalcemia was reported in less than 1% of a

**TABLE 1**  
**Patient Survival and Pathological Characteristics**

	Survival after diagnosis of hypercalcemia	Pathological features
Ballard <sup>1</sup>	19 days	Myelofibrosis Metastatic calcification 2 normal parathyroids
Ballard <sup>1</sup>	5 weeks	
Steinberg <sup>2</sup>	3 months	Myeloblastoma
Haskell <sup>3</sup>	4 months	4 normal parathyroids
Haskell <sup>3</sup>	14 days	Leukemic infiltrates Metastatic calcification 1 normal parathyroid
Licht <sup>4</sup>	28 days	Myelofibrosis
McKee <sup>5</sup>	Exact time not reported	Leukemic infiltrates Metastatic calcification 3 normal parathyroids
Rasheed <sup>6</sup>	1 month	Leukemic infiltrates Metastatic calcification
Present Case	2 months	Myelofibrosis Leukemic infiltrates Metastatic calcification 3 normal parathyroids

**TABLE 2**  
**Clinical Characteristics**

Authors	Age	Sex	Peak Calcium mg/dl	Lytic Bone Lesions	Bone Pain	Interval from diagnosis of CML to onset of hypercalcemia
Ballard, Marcus <sup>1</sup>	31	M	14.3	+	+	4 months
Ballard, Marcus <sup>1</sup>	40	M	21.5	+	+	53½ months
Steinberg, et al. <sup>2</sup>	40	M	15.0	+	+	11 months
Haskell, et al. <sup>3</sup>	44	F	12.1	+	+	33 months
Haskell, et al. <sup>3</sup>	52	M	13.8	—	+	38 months
Licht, et al. <sup>4</sup>	40	F	14.2	+	+	63 months
McKee, et al. <sup>5</sup>	58	M	16.0	—	—	4 years
Rasheed, et al. <sup>6</sup>	64	M	15.0	—	+	14 months
Present case	42	F	17.4	+	+	56 months



large series of lymphoma and leukemia patients.<sup>1</sup> Eight cases of hypercalcemia developing in the course of CML have been reported (Table 1).<sup>2-7</sup> In CML, hypercalcemia is discovered as the leukemia enters the acute or subacute stage. Median survival is one month following discovery of the hypercalcemia (Table 2). Six of nine patients (including this report) have demonstrated multiple, punched-out, lytic bone lesions on X-ray. One such lesion was biopsied and found to be composed of sheets of myeloblasts.<sup>3</sup> Autopsy findings have generally included ectopic calcification, normal parathyroid glands and widespread infiltration of organs with leukemic cells.

To the best of our knowledge, measurement of serum PTH has not previously been reported in a case of CML with hypercalcemia. In our patient the level of serum PTH fell within the normal range for persons with normal serum calcium. For a patient with hypercalcemia it was inappropriately elevated. Primary hyperparathyroidism was excluded by failure to find adenomatous or ectopic parathyroid tissue at autopsy. The serum levels of calcium and PTH in our patient were characteristic of ectopic hyperparathyroidism by the criteria of Riggs et al.<sup>9</sup>

Ectopic hyperparathyroidism appears to be the main cause of the hypercalcemia of cancer. One-hundred-eight unselected hypercalcemic patients with cancer were tested and 95.3% found to have inappropriately elevated PTH, even those with clinically evident bone metastases.<sup>10</sup> Benson et al. concluded that in only a few cases were mechanisms other than ectopic hyperparathyroidism necessary to explain the hypercalcemia.<sup>10</sup>

Evidence for ectopic hyperparathyroidism was found in three cases of acute leukemia and hypercalcemia.<sup>11-13</sup> In one of these patients, both the high serum levels of calcium and PTH reverted to normal during repeated, induced remissions and rose again during relapses.<sup>12</sup> Leukemic cells from this patient secreted PTH *in vitro*.<sup>12</sup> Serum PTH levels in all three of these cases supported the hypothesis of production of PTH by the leukemic cells.

A possible mechanism for the production of PTH by leukemic cells is explained by the hypothesis of genetic derepression.<sup>14</sup> This depends on the fact that each cell has a full complement of DNA and, therefore, the potential to produce any normal polypeptide. Normal cells are thought to have repressors that prevent the expression of those structural genes whose products are not needed by the cell. Cancer cells may have

deranged genetic controls, allowing the derepression of certain genes and the production of polypeptides not usually elaborated by the normal cells of origin. The appearance of a new, less mature clone of malignant cells with deranged genetic controls enables them to produce an ectopic hormone such as PTH. This mechanism may be operative in causing the hypercalcemia of CML.

The biological activity of the immunoreactive PTH in the serum of hypercalcemic patients with malignancy must be demonstrated before it is proven that ectopic hyperparathyroidism is the cause of the hypercalcemia.<sup>15</sup> The active site of PTH is known to reside in the amino terminal end of the molecule.<sup>16</sup> Detection of immunoreactive PTH with a carboxy terminal-specific assay by itself does not prove it is the cause of hypercalcemia: inactive carboxy terminal fragments are detected as well as the intact molecule.

Theoretically the best treatment of cancer-related hypercalcemia is treatment of the underlying malignancy. Resolution of hypercalcemia with removal of solid tumors has been reported.<sup>20</sup> Satisfactory control of hypercalcemia in leukemia depends on successful chemotherapy and has been attained in the cases reported by Zidar et al,<sup>12</sup> and Jayaraman and David.<sup>13</sup> The generally unfavorable results of treatment for the acute stage of CML and the rarity of associated hypercalcemia make it difficult to assess the effect of chemotherapy on serum calcium levels. Emergency measures directed at lowering the serum calcium are temporarily helpful. Hydration, corticosteroids, oral and intravenous phosphates and calcitonin are useful in controlling the severe hypercalcemia. Mithramycin, a cytotoxic antibiotic may be helpful in lowering hypercalcemia, probably by a direct effect on bone resorption, which inhibits RNA syntheses in osteoclasts. Vincristine, a cytotoxic vinca alkaloid, has been useful in the treatment of blastic transformation of CML. In our patient this drug was temporarily effective in controlling the hypercalcemia. The favorable response of our patient's hypercalcemia to cytotoxic drugs further supports the ectopic production of PTH by her leukemic cells.

Clinical deterioration in a patient with CML may be explained by rapidly developing hypercalcemia. When hypercalcemia precedes overt blastic transformation of CML it may be a marker of that transformation. We suggest that the hypercalcemia in this patient with CML may have been due to the elaboration of PTH by leukemic cells.

References will be found on page 242.



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# Clinically Unsuspected Insulinoma

GEORGE R. DINYER, M.D.\* and DEREK OLDENBURGER, M.D., F.A.C.P.†

A 25-year-old woman with an eight year history of mental illness characterized by episodic hysterical behavior was found to have "reactive hypoglycemia" on oral glucose tolerance testing. After a high-protein diet was noted to exacerbate her symptoms, a repeat oral glucose tolerance test was done with plasma immunoreactive insulin. Her peak plasma immunoreactive insulin (IRI) value was 1300  $\mu$ U/ml at one and one-half hours with a corresponding plasma glucose level of 59 mg/dl. At three hours her plasma IRI value was 279  $\mu$ U/ml with a plasma glucose level of 24 mg/dl with observed anxiety, diaphoresis and fine tremor. Subsequently, a 3 cm islet cell tumor in the tail of the pancreas was removed, and the patient's symptoms subsided. Plasma immunoreactive insulin drawn whenever hypoglycemia is noted during oral glucose tolerance testing may be helpful in diagnosing clinically unsuspected insulinomas.

**T**HE TYPICAL PATIENT with an insulinoma presents with early morning or late afternoon symptoms which may include sweating, weakness, palpitations, visual disturbances and mental changes.<sup>1</sup> Our patient's mental disturbances during hypoglycemia were her predominant clinical symptoms leading to psychiatric treatment and the diagnosis of hysteria. She was thought to have reactive hypoglycemia by oral glucose tolerance testing. However, when this was combined with plasma immunoreactive insulin levels, the correct diagnosis soon became evident.

## Case Report

A 25-year-old woman occupational therapist was seen with an eight-year history of intermittent "attacks" of tremor, diaphoresis and anxiety. Eight years prior she had spent one week in a psychiatric ward for treatment of hysteria.

The attacks during the last eight years have occurred indiscriminately and have had no definite relationship to eating. Approximately six months prior to admission she had one brief episode in the morning which resolved after a few minutes, untreated. On another occasion in the morning, she drank a glass of juice which seemed to alleviate her symptoms. A standard 75 gram three-hour glucose tolerance test was done which revealed a blood sugar level of 23 mg/dl at three hours. At that time she became lightheaded and agitated. She was then placed on a high-protein diet which aggravated her symptoms.

On two occasions she was seen in the emergency room of the hospital complaining of diaphoresis, tremor and anxiety at which time plasma glucose determinations were 50 and 52 mg/dl,

respectively. She was given intravenous glucose which alleviated her symptoms. A repeat three-hour glucose tolerance test was performed with simultaneous plasma insulins and revealed a peak serum IRI value of 1300  $\mu$ U/ml at one and one-half hours (Figure), normal fasting value (0-25  $\mu$ U/ml). The patient was hospitalized.

Physical examination revealed a young woman in no acute distress who was 163 cm (five feet four inches) in height and weighed 61.2 kg (135 pounds). There were no abnormal physical findings. Results of routine laboratory studies including complete blood count and

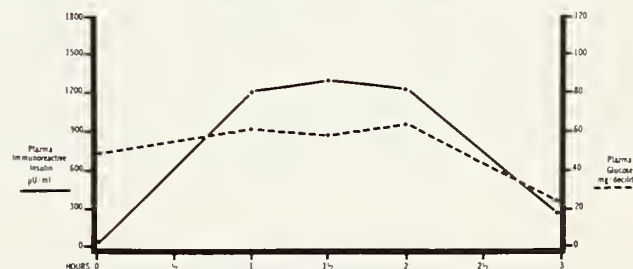


Figure — Glucose tolerance test with plasma immunoreactive insulin determinations.

urinalysis as well as SMA-12/60 autoanalysis were normal. A fast was begun and at 24 hours the patient became anxious, cried and was tremulous. Her plasma glucose level at that time was 28 mg/dl and her plasma insulin level was 30.2  $\mu$ U/ml. Subsequently, angiographic studies revealed a tumor located in the tail of the pancreas. A 3 x 2.8 x 2.2 cm islet cell tumor was removed surgically. Postoperatively the patient's plasma glucose level returned to normal and she became asymptomatic.

## Comment

The diagnosis of an insulinoma in a patient with typical symptoms and fasting hypoglycemia is not difficult. The recent use of serum C-Peptide immunoactivity and insulin binding antibodies has

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facilitated the evaluation of patients suspected of having factitious hypoglycemia.<sup>2</sup> Two patients with a non-autonomous functioning insulinoma have been reported who never developed fasting hypoglycemia.<sup>3,4</sup> Both of these patients had exaggerated insulin responses following oral glucose. Although our patient's extreme insulin response following oral glucose is very unusual, values in the hundreds of microunits per milliliter are not uncommon.<sup>5</sup>

It is well known that the diagnosis of an insulinoma frequently is not made until several years have elapsed

from the onset of symptoms.<sup>1</sup> The use of a plasma immunoreactive insulin drawn during oral glucose tolerance testing whenever hypoglycemia is noted may lead to the finding of an insulinoma when it is unsuspected.

Elevated IRI levels occur during hypoglycemia after glucose tolerance testing in early diabetes mellitus.<sup>6</sup> Whenever the glucose tolerance curve is non-diabetic and the plasma IRI is inappropriately elevated during hypoglycemia, further diagnostic evaluation is suggested.

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# Chronic Obstructive Pulmonary Disease and Secretory IgA

HORACE H. ZINNEMAN, M.D.\*; DENNIS E. NIEWOEHRER, M.D.\* and MARILYN G. GOODSSELL, M.D.\*

**Contradictory reports on the relation of sIgA concentration to COPD prompted this study of a larger group of patients. Data gained from serum, saliva and sputum of 91 male patients with COPD failed to find causal relation of sIgA concentration to the disease or its extent. Thus, although COPD is frequently found in patients with immunoglobulin defects, a reciprocal statement cannot be made.**

**T**HE HIGH INCIDENCE of chronic bronchitis, bronchiectasis and chronic obstructive pulmonary disease (COPD) in patients with immunoglobulin deficiencies lent itself to the speculation, that a decrease or deficiency of secretory IgA might be a significant factor in COPD. Several studies have been addressed to that question, measuring circulating IgA, sIgA or both.

Medici and Buergi<sup>1</sup> analyzed the sputa of 34 patients with COPD of various severity. They reported a significant decrease of IgA and secretory component (SC) only in seven patients with far advanced disease, whereas IgA was increased in patients with lesser disease. Another report by Falk et al. of the same year<sup>2</sup> also found decreased IgA with a concomitant increase of IgG in the sera of patients with COPD of long duration. Later on the same group of investigators studied six patients with COPD and found one of them completely deficient of IgA.<sup>3</sup> Secretory component was not measured in that particular study.

Other investigators however found IgA concentrations in serum or sputum of patients with COPD normal or even increased.<sup>4-9</sup> Some of these studies found abnormal IgM or IgG concentrations in either serum or sputum, but only one study tested concentrations of SC. It was found to be absent in patients with severe disease of long duration.

Since all of these studies dealt with small numbers of patients, those contradictory reports are difficult to evaluate, particularly considering the difficulties of obtaining valid sputum specimens. For these reasons we considered it worthwhile to study concentrations of

immunoglobulins as well as SC and  $\alpha_1$ -antitrypsin in 91 patients with COPD.

## Materials and Methods

Ninety one male patients of the pulmonary outpatient clinic at the Minneapolis Veterans Medical Center were studied. Their ages ranged from 48 to 83 years. All patients had an FEV<sub>1.0</sub> less than 60% of predicted and otherwise had clinical and laboratory findings consistent with irreversible airflow obstruction. Patients with other associated pulmonary conditions, those with known malignancies, and those receiving immunosuppressive drugs were excluded. They could be divided into three groups according to pulmonary function, which had been tested repeatedly for each of the patients. Group I comprised 9 patients with FEV<sub>1</sub> < 0.5 liter, group II counted 49 patients with FEV<sub>1</sub> of 0.5 to 1.0 liter, and group III with 33 patients with FEV<sub>1</sub> > 1.0 liter.

Sputa, collected from a deep cough were homogenized with 0.1 ml of acetyl cysteine and either tested immediately or frozen at -20°C until tested. Immunoglobulins A, M and G of serum, saliva and sputa were measured in sol state by single radial immune diffusion on commercially prepared plates. (Behring Werke, GMBH) serum  $\alpha_1$ -antitrypsin levels also were determined by single radial immune diffusion on plates by the same firm. Low level plates were employed whenever the standard plates failed to show precipitation rings. Standards for secretory IgA (sIgA) had been prepared by injection of human colostral sIgA into rabbits. The harvested rabbit serum was then absorbed with human  $\gamma$  and  $\mu$  chains. Presence of SC in saliva and sputum was observed by

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double immune diffusion, using anti-SC goat serum (Behring Werke, GMBH).

### Results

None of the patients were partly or totally deficient in  $\alpha_1$ -antitrypsin. Serum immunoglobulins in all but one patient were found to be within the range, which had been established previously in our laboratory for normals. The patient with known dysgammaglobulinemia showed a dichotomy between serum and sputum immunoglobulins: The serum levels were IgG 27 mg/dl, IgA 0, IgM 7.0 mg/dl. Sputum levels were as follows: IgG 46 mg/dl, IgA 100 mg/dl, IgM 118 mg/dl.

Sputum concentrations of sIgA were slightly lower in patients with more severe disease, but not significantly so by student t-test.

Correlation coefficients of per cent predicted FEV<sub>1</sub> with IgA, IgG and IgM of serum (Table 1), saliva (Table 2) and sputum (Table 3) were in no case significant at the level of  $p < 0.5$ . SC was present in all salivary and sputum specimens.

### Comment

This study was undertaken in the hope that results

derived from a greater number of patients might clarify contradictory reports of previous studies. One of the difficulties inherent in all studies is the contamination of sputum by saliva, except in cases where sputum can be obtained from tracheotomies or by bronchoscopy. For this reason we studied both saliva and sputa. The difficulty of obtaining valid sputa from normal persons made it necessary to dispense with control specimens of equal numbers for comparison.

Conversion of sputum to the sol-state is necessary in order to obtain meaningful recovery of immunoglobulins, because mucin fibrils of the gel state will trap immunoglobulins. In this study the sol state was accomplished by incubation with acetyl cysteine. The presence of SC was established qualitatively by double immune diffusion, in order to verify the presence of sIgA and to rule out significant exudation of serum IgA through inflamed or denuded bronchial mucosa. The presence of SC also rules out deficiency of the component, a rare occurrence described previously.<sup>10,11</sup>

Patients of groups I, II, and III were compared for possible differences of immunoglobulin concentrations according to severity of the disease. Immunog-

TABLE 1

#### Serum Components of 91 Patients with COPD

	9 patients (av. age 75 y) with FEV <sub>1.0</sub> <0.5 l mean values	49 patients (av. age 65 y) with FEV <sub>1.0</sub> 0.5-1.0 l mean values	33 patients (av. age 70 y) with FEV <sub>1.0</sub> >1.0 l mean values
$\alpha_1$ Antitrypsin	321 mg/dl	316 mg/dl	380 mg/dl
IgG	1091 mg/dl	1162 mg/dl	1291 mg/dl
IgA	319 mg/dl	315 mg/dl	294 mg/dl
IgM	123 mg/dl	153 mg/dl	171 mg/dl

TABLE 2

#### Immunoglobulins in the Saliva of 91 Patients with COPD

	9 patients (av. age 75 y) with FEV <sub>1.0</sub> <0.5 l mean values	49 patients (av. age 65 y) with FEV <sub>1.0</sub> 0.5-1.0 l mean values	33 patients (av. age 70 y) with FEV <sub>1.0</sub> >1.0 l mean values
IgG	2.6 mg/dl	2.6 mg/dl	2.21 mg/dl
IgA	55.5 mg/dl	49.0 mg/dl	59.5 mg/dl
IgM	0 mg/dl	0.2 mg/dl	0. mg/dl
SC*	+	+	+

\*Secretory component

TABLE 3

#### Immunoglobulins in the Sputa of 91 Patients with COPD

	9 patients (av. age 75 y) with FEV <sub>1.0</sub> <0.5 l mean values	49 patients (av. age 65 y) with FEV <sub>1.0</sub> 0.5-1.0 l mean values	33 patients (av. age 70 y) with FEV <sub>1.0</sub> >1.0 l mean values
IgG	3.9 mg/dl	12.7 mg/dl	19.6 mg/dl
IgA	158.0 mg/dl	186.0 mg/dl	238.0 mg/dl
IgM	1.6 mg/dl	9.15 mg/dl	10.0 mg/dl
SC*	+	+	+

\*Secretory component



lobulin concentrations, particularly of sIgA showed no correlation with severity or duration.

The results of this study suggest strongly, that

COPD is not commonly associated with deficiency or decrease of sIgA, even in advanced stages of the disease.

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# The Middle Cranial Fossa Approach to the Temporal Bone

STEPHEN G. HARNER, M.D.\* and EDWARD R. LAWS, JR., M.D.†

**Harner SG, Laws ER Jr: The middle cranial fossa approach to the temporal bone.**

The middle cranial fossa approach to the temporal bone is useful for certain neuro-otologic disorders; six representative cases are reported. The most common current indication for this approach is sectioning of the vestibular nerve for relief of vertigo in Meniere's syndrome. Complications include cerebrospinal fluid fistulas and facial paresis.

**T**HE MIDDLE CRANIAL fossa approach to the temporal bone has been utilized for many years. Among the first reports was that of Parry,<sup>1</sup> who used this route for section of the eighth nerve in a patient with Meniere's syndrome. Unfortunately, he also sectioned the seventh nerve, and this left the patient with a permanent facial paralysis.

The concept of intracranial vestibular nerve section was first popularized by Dandy.<sup>2</sup> He operated on approximately 600 patients with Meniere's syndrome, using the posterior fossa approach. Initially only a portion of the nerve was sectioned, and later, the entire nerve. Long-term follow-up showed a 90% success rate for relief of vertigo.<sup>3</sup> These procedures were done without the aid of the operating microscope. Other surgeons tried his procedure but apparently were unable to duplicate his results.

Middle fossa craniotomy has remained a standard neurosurgical approach, utilized for operations on the trigeminal ganglion and sensory root for tic douloureux. It was not used extensively for temporal bone procedures. Until 1961, there were occasional reports of the middle fossa approach being used for petrositis, fenestration of the superior semicircular canal (for otosclerosis), repair of the facial nerve, reconstruction of the tegmen tympani after fractures, and sectioning of the greater superficial petrosal nerve.<sup>4</sup> In 1961, House<sup>5</sup> used modern microsurgical techniques to open the internal auditory canal through the middle cranial fossa and to section the vestibular nerve without damaging the cochlear nerve or the

facial nerve. In 1963, he<sup>6</sup> expanded his indications for use of this method to include the removal of small intracanalicular acoustic neuromas. Since that time, several authors have reported on the use of the middle cranial fossa approach to the temporal bone in patients with Meniere's syndrome, facial neuromas, facial paralyzes, various tumors of the temporal bone, trigeminal neuralgia, and cerebrospinal fluid fistulas.<sup>4,7,8</sup> We present representative cases in which the middle cranial fossa approach was used.

## Case Reports

### Case 1.

In September 1975, a 28-year-old man presented with sensorineural hearing loss, tinnitus, and fullness in the left ear. He also had episodic vertigo. Complete workup including a positive contrast rhombencephalogram of the posterior fossa led to a diagnosis of Meniere's syndrome. A Cody tack procedure was performed.<sup>9</sup> The patient noticed some improvement initially; however, over the next year, he became totally incapacitated. A destructive labyrinthectomy was recommended. The patient refused because he was reluctant to lose the hearing in that ear; at this time he had a hearing loss of 70 dB. A middle fossa section of the vestibular nerve was performed on June 7, 1977. The procedure was uncomplicated. His postoperative course was similar to that of a destructive labyrinthectomy, with nausea, vomiting, and vertigo occurring through the first several days. There was a complete ipsilateral peripheral facial paresis. He was dismissed from the hospital on the fifth postoperative day and was able to navigate with minimal difficulty by the end of the week. On follow-up examination in May 1978, he stated that he had had no further vertigo. The hearing was unchanged, and there was still residual facial weakness without synkinesis. The patient now leads a normal life. He and his wife are very satisfied with the result of the procedure.

### Case 2.

A 59-year-old man had a chondroblastoma of the temporal bone. Complete evaluation showed an extensive tumor arising in the region

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of the mastoid antrum; it extended through the middle ear and along the floor of the middle cranial fossa medially toward the internal carotid artery (Figure 1). He had a mixed hearing loss of 70 dB but no other neurologic deficit. This tumor was approached by means of a combination of middle cranial fossa craniotomy and mastoidectomy. Gross total removal of the tumor was accomplished. The facial nerve had been widely exposed, but the patient did not have any facial palsy after operation. No recurrence was apparent at follow-up examination in June 1978, 1 year after surgery.

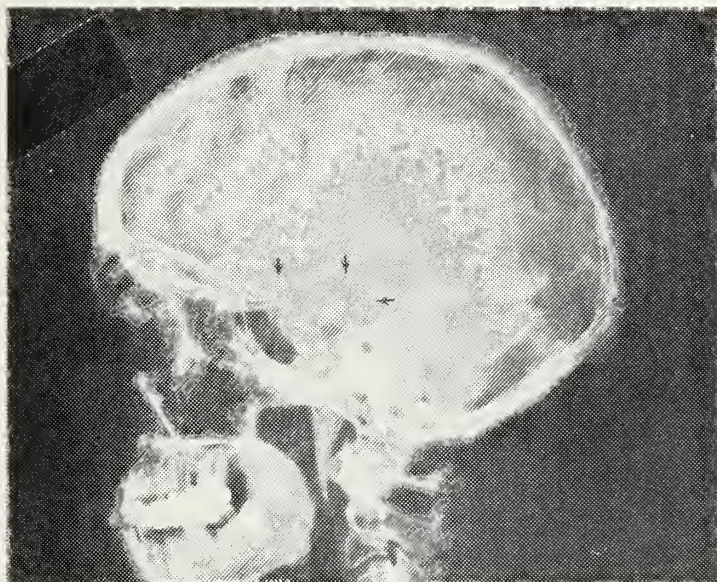


Fig. 1 (Case 2) — Lytic defect in temporal bone (arrows).

#### Case 3.

A 68-year-old man had a three-year history of facial palsy on the left side. In addition, he had a mixed hearing loss, a questionable history of otorrhea, and no vertigo. Tomograms revealed a destructive lesion medial to the superior semicircular canal in the region of the internal auditory canal (Figure 2). Caloric testing revealed no response in the left labyrinth. It was thought that he most likely had a facial nerve neuroma arising in the internal auditory canal. This was approached through a middle cranial fossa craniotomy. A large cholesteatoma was found; it filled the internal auditory canal and extended into the region of the epitympanum laterally and into the posterior cranial fossa medially. The



Fig. 2 (Case 3) — Destructive lesion medial to superior semicircular canal (arrow).

cholesteatoma was removed in its entirety. The defect was closed with the use of a muscle flap and dural homograft. Postoperatively, the patient had mild disequilibrium and transient drainage suggestive of cerebrospinal fluid. These resolved spontaneously. He was dismissed from the hospital at the end of one week; his postoperative course was uneventful. In March 1979 he had a hypoglossal-facial nerve anastomosis.

#### Case 4.

A 55-year-old man had recurrent meningitis and cerebrospinal fluid otorrhea. He had a long history of chronic otitis media on the right and had undergone a tympanoplasty 10 years previously. He had had two episodes of pneumococcal meningitis, five and three years previously. Physical examination revealed cerebrospinal fluid leaking through a polyethylene tube in the right tympanic membrane. We used the middle fossa approach and exposed a defect of 5 by 4 mm in the floor of the middle fossa. The dura was deficient over the defect; it was repaired with a pedicle graft of temporalis muscle which was sutured to the dural margin. Postoperatively, hearing was preserved and no further leakage of cerebrospinal fluid was noted. However, the patient had another episode of pneumococcal meningitis 16 months after surgery. Following recovery from this, he was symptom-free at last report two years after the last operation.

#### Case 5.

A 61-year-old woman was seen who had a one-year history of disequilibrium and progressive paresis of the right facial nerve. Examination revealed mild ataxia, complete peripheral facial palsy on the right, and loss of the sense of taste. By means of a middle fossa approach, we exposed a 3-cm encapsulated tumor breaking through the floor of the middle fossa. Gross total removal of a neurilemoma arising from the facial nerve was accomplished. A hypoglossal-facial anastomosis was performed. Her postoperative course was satisfactory. Hearing was preserved and facial nerve function was excellent. She remained well at 18 months after surgery.

#### Case 6.

A 13-year-old girl had experienced putulent otorrhea on the right at the age of six years. A cholesteatoma was found and mastoidectomy was performed. At nine years of age, an ear infection developed, with meningitis and seizures. She subsequently had ear surgery that involved removal of recurrent cholesteatoma. At age 11 years, operation was performed to correct "sagging" of the ear canal. On admission to our institution, she had decreased hearing, stenosis of the external auditory canal, a mass in the middle ear, and cerebrospinal fluid otorrhea. Tomography showed a posttraumatic encephalocele in the middle fossa. A right middle fossa approach was employed, and a 15-mm dehiscence was discovered in the floor of the middle fossa. Brain and deficient dura had herniated through the defect. The dura was repaired primarily and reinforced with a pedicle graft of temporalis muscle. No cholesteatoma was present. Her postoperative course was uneventful; hearing was preserved and no leakage of cerebrospinal fluid was noted during the one-year follow-up since the last operation.

### Technique

The basic concept of this procedure is exposure of the superior surface of the petrous pyramid, using a temporal craniotomy. This makes the procedure extradural and extralabyrinthine. The patient is placed in the supine position and the head is turned to the side. A temporal craniotomy is performed just above the



external auditory canal and the dura of the temporal lobe is retracted medially. Removal of cerebrospinal fluid by means of a malleable spinal needle may be desirable. A self-retaining retractor (House-Urban) is inserted. The surgeon sits at the head of the table and examines the superior surfaces of the temporal bone. The major landmarks used are the superior petrosal sulcus, the arcuate eminence (superior semicircular canal), the hiatus of the facial canal with the greater superficial petrosal nerve, and the foramen spinosum with the middle meningeal artery (Figure 3 and 4). The usual procedure is to identify and expose the internal auditory canal. Occasionally, a tumor may have eroded through the floor of the middle fossa; this makes identification easy. If no erosion is apparent, two basic methods may be used to localize the internal auditory canal. The first is to trace the greater superficial petrosal nerve to the geniculate ganglion of the facial nerve. This is located by using the hiatus of the facial canal and the foramen spinosum as landmarks. The bone over the greater superficial petrosal nerve is removed to the geniculate ganglion. The facial nerve is then traced between the superior

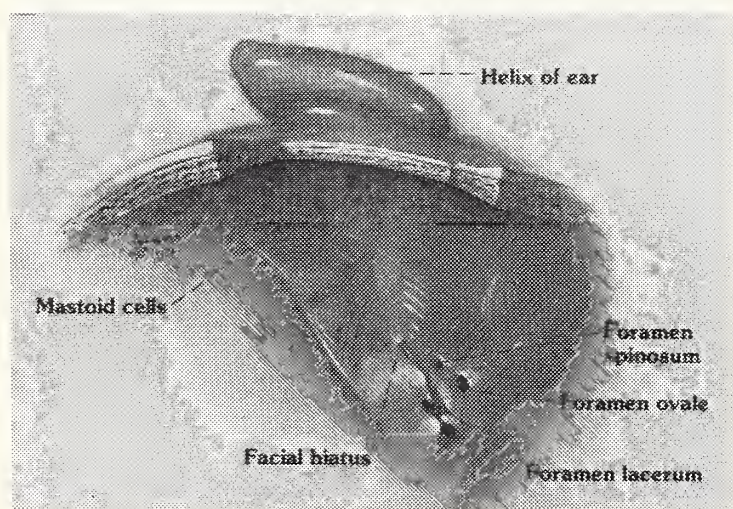
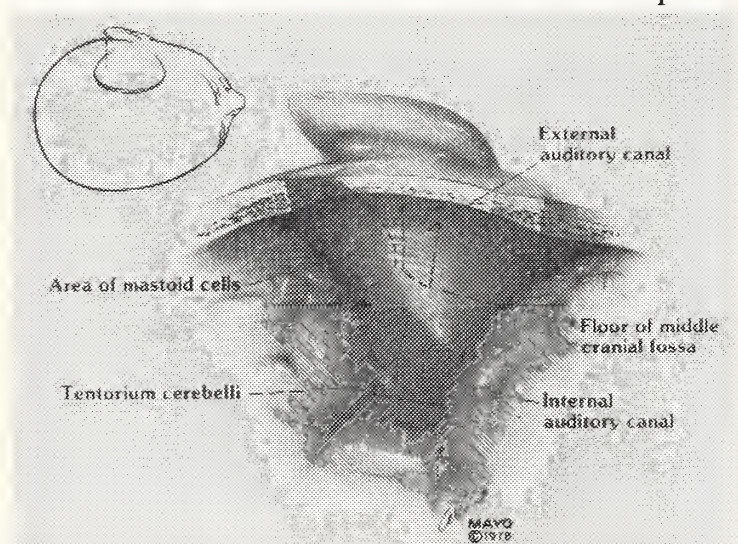


Fig. 3 — (A-top) and (B-bottom), Superior surface of temporal bone as seen at operation.

semicircular canal and the basal turn of the cochlea (labyrinthine segment) into the internal auditory canal. This is the method described by House<sup>5</sup> and it is used by many surgeons.

The second method is that described by Fisch.<sup>4</sup> His technique is to identify the arcuate eminence first; this is the bony covering of the superior semicircular canal. He stated that it lies at an angle of 90° to the superior petrosal sulcus. Using those two constant landmarks, he suggested visualization of an imaginary line from the anterior end of the superior semicircular canal to the superior petrosal sulcus. The angle between that imaginary line and the plane of the superior semicircular canal is approximately 60°. The triangle formed by this imaginary line, the semicircular canal, and the superior petrosal sulcus is the sheet of bone which overlies the internal auditory canal. Approaching the internal auditory canal by this method reduces the risk of injury to the facial nerve and cochlea.

Regardless of which method is used, the internal auditory canal is exposed by using a drill, continuous suction, and the operating microscope (Figure 5). The dura is opened and the nerves are exposed (Figure 6). The nerves within the internal auditory canal have a constant relationship (Figure 6 *inset*). Seen from above, the anterior nerve is always the facial nerve, which is more superficial than the posteriorly located vestibular nerve. The superior and inferior divisions of the vestibular nerve arise from Scarpa's ganglion and ultimately form a single nerve; the cochlear nerve is anterior and inferior, and using this approach, one should rarely have to be concerned about it. Another constant finding is the presence of small anastomoses between the vestibular and facial nerves.<sup>4</sup> Rhoton<sup>10</sup>

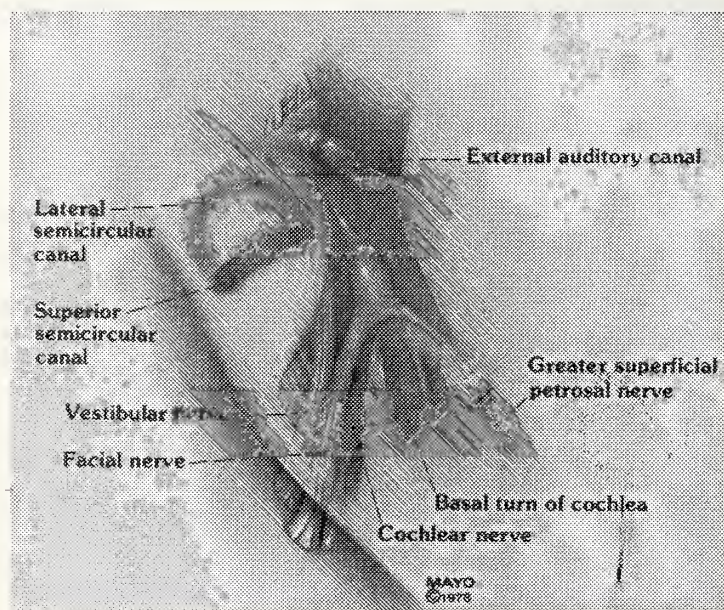


Fig. 4 — Close-up of same area as Figure 3, showing operative details.



believes that the major anastomosis is the nervus intermedius traveling initially with the vestibular nerve and crossing to the facial nerve in the internal auditory canal. Before cutting and removing a segment of the vestibular nerve, one must sever these anastomotic attachments to avoid traction on the facial nerve (Figure 7).

Once the internal auditory canal has been opened,

three procedures are possible. The first is vestibular neurectomy, which is accomplished by identifying the vestibular nerve from above and cutting the superior and inferior divisions and the distal singular branch as close to the labyrinth as possible (Figure 8). Medially the vestibular nerve is sectioned so that a segment may be removed. In earlier years, some surgeons sectioned only the superior division of the vestibular nerve which

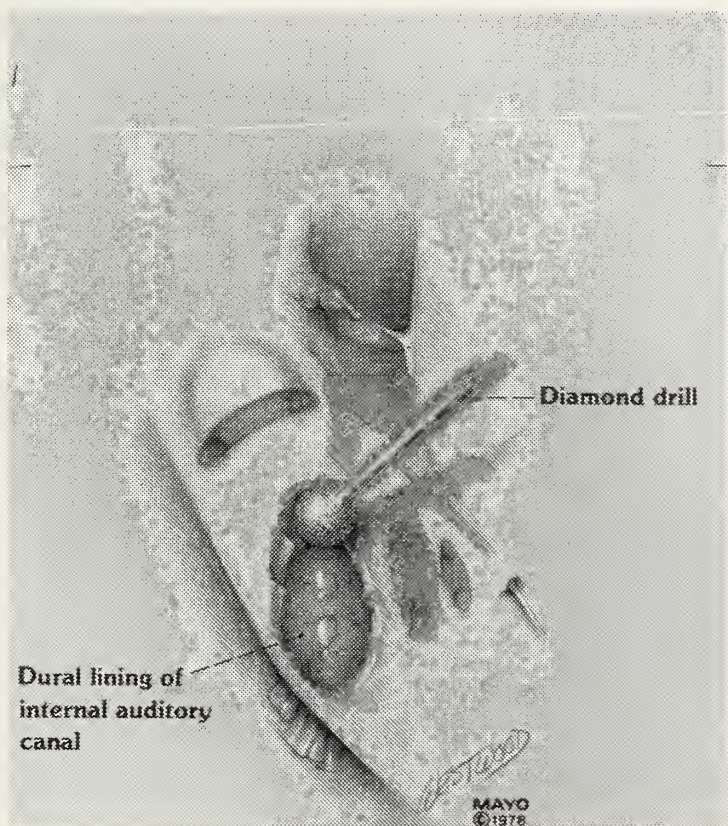


Fig. 5 — Drilling to expose internal auditory canal.

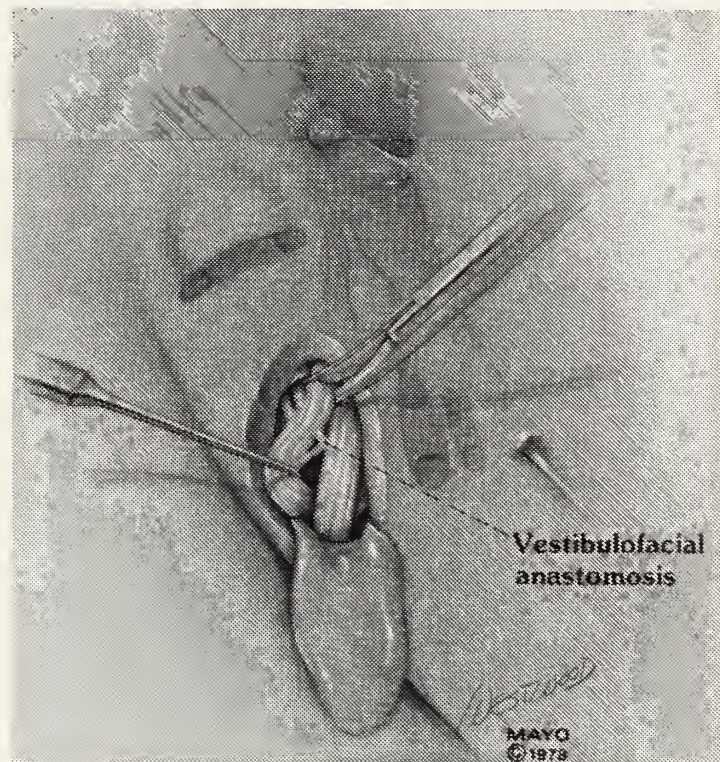


Fig. 7 — Cutting vestibular nerve.

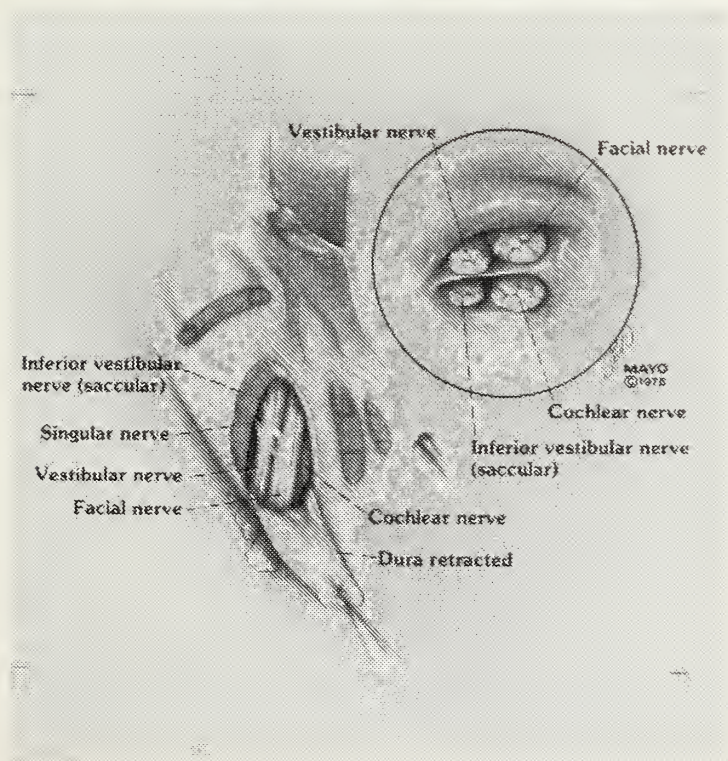


Fig. 6 — Contents of internal auditory canal. *Inset* shows alignment of nerves in internal auditory canal.

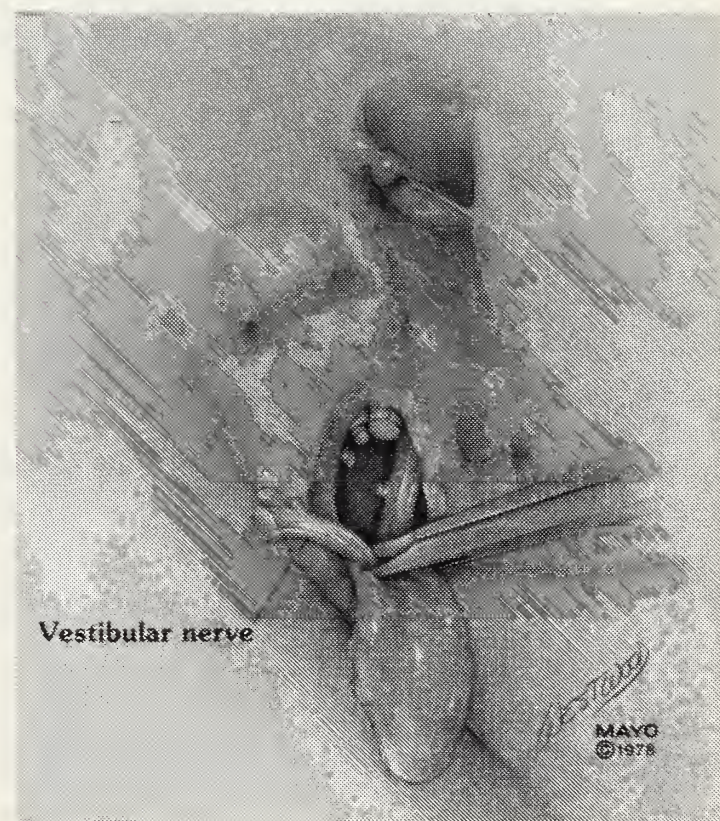


Fig. 8 — Removing segment of vestibular nerve.



supplies the utricle and the superior and horizontal semicircular canals. In most cases, this is adequate. Failure of the procedure is thought to be due to incomplete section of the nerve.

A second procedure that can be performed is exploration of the internal auditory canal. This would be appropriate for tumors of the facial nerve or for small acoustic neuromas that lie completely within the internal auditory canal and might be approached more easily by this means than by the traditional posterior fossa approach.

A third procedure is exposure of the facial nerve in the meatal and labyrinthine segments. This is indicated in cases of trauma with fracture of the temporal bone and secondary facial paralysis. If it is uncertain whether the nerve has been traumatized or sectioned, these areas can be exposed, and the nerve can be repaired as indicated.

### Indications

Dandy<sup>2</sup> reported excellent control of Meniere's syndrome with vestibular nerve section. Other surgeons tried to duplicate his technique<sup>11</sup> but frequently were unable to cut the entire nerve without injury to the facial nerve or to the cochlear nerve or to both. About the same time, Day<sup>12</sup> developed the destructive labyrinthectomy, which could be performed by the otologic surgeon. It avoided the risks of an intracranial procedure, but the major disadvantage was that the patient would lose the hearing in the affected ear.

Since surgeons have resumed use of the middle fossa approach to the temporal bone, the procedure most commonly performed has been section of the vestibular nerve for treatment of Meniere's syndrome. Another recognized indication for its use is the small intracanalicular acoustic neuroma.<sup>6</sup> This indication is questioned by some surgeons, because preoperative evaluation sometimes fails to reveal the exact size of the tumor. Tumors that extend medial to the internal auditory meatus are difficult to remove by the middle fossa approach. Currently, these tumors are approached via the posterior fossa. A variety of facial nerve disorders are amenable to the middle fossa approach. Temporal bone fractures, as well as facial neuromas, that are medial to the geniculate ganglion can be approached and corrected satisfactorily by this method. Vertigo that arises as a complication of surgery of the middle ear or as the result of trauma to the head is better controlled by a procedure that cuts the vestibular nerve medial to Scarpa's ganglion. Other recognized indications for the middle fossa approach include the various tumors that arise within the

temporal bone and extend to or into the middle cranial fossa. Petrositis that cannot be completely exteriorized through the mastoid can be approached by way of the middle cranial fossa. In many cases, cerebrospinal fluid otorrhorrhea may be corrected by this method of exposure.

### Complications

The most commonly recognized complications of the middle cranial fossa approach are cerebrospinal fluid fistulas and facial paresis.<sup>4,11,13</sup> Cerebrospinal fluid fistulas have been seen in approximately 2% of the patients who have undergone this procedure. Most fistulas cease spontaneously; however, all surgeons who use this procedure admit that they have had to resort to surgical repair for some of these leaks. Facial paresis is seen in approximately 7% of the patients. Most authors report that this appears either immediately or within several days of the operation and resolves within weeks to months. Generally, even a severely traumatized facial nerve will recover a large amount of its function if it has not been sectioned. Significant loss of hearing is reported in approximately 10% of the cases, and persistent vertigo occurs in approximately 2%. Other rare complications include meningitis, intracranial hematoma, and seizures. The incidence of fatal complications after the use of the middle cranial fossa approach could not be accurately determined; however, it appears to be below 1%.

### Results

The results of the use of the middle cranial fossa approach to the temporal bone vary, depending on the indication for the procedure. Virtually 100% of the patients who are operated on for relief of vertigo should have resolution of their problem. When one labyrinth is lost, patients will experience a sense of falling as they turn rapidly to the affected side. In younger patients, this is a minor problem; in older patients, compensation may be incomplete. Patients who are operated on because of Meniere's syndrome generally have little change in their symptoms of tinnitus, fullness in the ear, or fluctuation in hearing loss. Because these are cochlear in origin, no change is expected. The cases of tumors, facial nerve paralysis, or related disorders are so diverse and the conditions occur in such small numbers that results achieved with the middle fossa approach are impossible to project. We know that the approach described gives us excellent exposure and the ability to perform a complete procedure in the patients who have been suitably chosen.



### Summary

The middle cranial fossa approach to the temporal bone has been known for many years. After a period of disuse, it was reintroduced in 1961 and has been updated by the use of the operating microscope and modern microsurgical techniques. By far the most

common indication for its use remains section of the vestibular nerve for Meniere's syndrome or other labyrinthine disorders. We believe that the middle cranial fossa approach is best accomplished by using the combined talents of the neurosurgeon and the otologic surgeon.

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# Tuberculous Meningitis in a Two-Year-Old Boy

DANIEL FIFE, M.D.\* and PAUL G. QUIE, M.D.†

**A case of tuberculous meningitis in a two-year-old Caucasian male is presented. His family harbored the disease for 25 years prior to his presentation. Many of the problems of diagnosis, therapy and public health often associated with tuberculosis in children are illustrated in this case.**

**T**UBERCULOSIS IN children is usually acquired from a close adult contact. Often this contact has known tuberculosis which is untreated or ineffectively treated.<sup>1,2</sup> In Caucasian employed populations in the developed nations, the illness is relatively rare.<sup>1,2,3,4</sup> Thus, the diagnosis may be missed or delayed.<sup>5,6</sup> The same rarity may lead to suboptimal control of the illness within the hospital, with occasionally diastrophic results.<sup>7</sup> We report a case of tuberculosis in which many of these problems are illustrated.

## Case Report

A two-and-a-half-year-old boy was transferred to the University

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## Tuberculosis in the Patient's Family

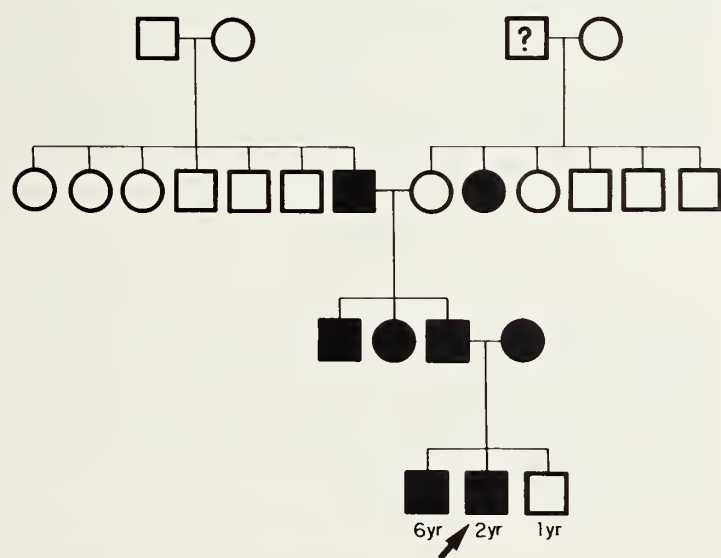


Figure — Hatched figures had active tuberculosis except for the patient's brother and mother who had converted skin tests but no other indication of tuberculosis. The figure marked "?" is the father's grandfather with possible tuberculosis. See text. □ male; ○ female.

of Minnesota hospitals because of a left sided seizure. He had been entirely well until one month before transfer, when he developed a fever to 102° F, accompanied by cervical lymphadenopathy and progressive lethargy and anorexia. For his first three weeks of illness his physician treated him as an outpatient. Urine analysis, chest Xray, mono spot and IVP were normal. Hemoglobin was 11.8 gm %, white blood cells were 17,900/mm<sup>3</sup> with 60 neutrophils, nine bands, 30 lymphocytes and one monocyte. Erythrocyte sedimentation rate was 66. Erythromycin and Keflex were each given for a week without improvement. Nine days prior to transfer he was hospitalized for persistent fever with progressive lethargy and anorexia. Pinworms were noted. A throat culture showed *Streptococcus pneumoniae*. Oral pyrimin pamoate (Povan) and penicillin were begun on the sixth hospital day. The patient began to vomit. Pyrimin pamoate was discontinued but vomiting persisted. By the day of transfer he was quite lethargic and anorexic and vomited frequently. His temperature had not exceeded 100° for three days.

## Family History

The patient had two brothers who were well. His father was a machinist and his mother a housewife. Both smoked and had chronic coughs. They lived and worked in a town 30 miles from Minneapolis. There were numerous household animals. On the initial interview, the father recalled that he had an aunt who had had untreated tuberculosis in the early 1950s. She had died some years before the patient was born. No other family history of tuberculosis was recalled at this time. Over the next three days, additional cases of tuberculosis in the family were remembered. The father's father had tuberculosis and had been treated. The father's sister had also had tuberculosis and been treated. The father's brother had a positive skin test and an abnormal chest Xray and had not been treated as far as the father knew. The father recalled that when he was a child, his maternal grandfather had died of an illness and that after death, his clothes and his mattress had been burned. The occurrence of tuberculosis in the family is diagrammed in the Figure.

## Findings and Clinical Course

On examination, the patient was a lethargic, pale child who tended to doze while being examined. Height was 87 cm; weight, 11.4 kgm; OFC, 49 cm; temperature, 99°; pulse, 80; respirations 26/minute; BP 110/60. The cervical nodes were shotty. The temporal margin of the right optic disk was blurred. The liver edge was three cm below the right costal margin. The neck was stiff. He followed commands but did not speak. He walked with assistance. Athetosis was noted. There was sustained clonus of all extremities and a bilateral Babinski sign. Tone was greater on the left side than on the right.



Cranial nerves were normal. The hemoglobin was 14.1 gm % and white count 24,000 with 74 neutrophils, 20 lymphocytes and 6 monocytes. Platelets were 743,000. Serum osmolality was 260 mOsm, Na<sup>+</sup> 126, K<sup>+</sup> 4.1, Cl<sup>-</sup> 85, HCO<sub>3</sub><sup>-</sup> 28, BUN <5, Creatinine <0.5, glucose 86. Urinary osmolality was 277 mOsm, Na<sup>+</sup> 64 and K<sup>+</sup> 27. Normal were urinalysis coagulation studies, chest Xray and skull Xray. CAT scan of the head showed hydrocephalus but no mass. A spinal tap was done and showed 62 WBC/mm<sup>3</sup> with 6 neutrophils and 57 mononuclear cells. No red cells were present. CSF protein was 128 mgm %, glucose 15 mgm % and Cl<sup>-</sup> 104 meg/1. Gram and AFB stains and India ink preparation were negative on the CSF. The working diagnosis the first hospital day was partially treated meningitis; rule out viral meningitis, tumor and tuberculosis. The patient was begun on ampicillin 550 mgm IV Q 6 hours and chloramphenicol 300 mgm IV Q 6 hours.

With the growing evidence for tuberculosis, skin tests were placed on both parents on the second hospital day. Both parents had negative skin tests in 1968. Both of the parents' skin tests were positive on the third hospital day. Chest Xrays were done. The mother's was normal, but the father's was abnormal with streaky infiltrates in both apices. His sputum was subsequently found to be positive for tuberculosis on smear and culture. The organism was multiply sensitive, its sensitivities included INH, PAS and rifampin and streptomycin. At this point, the evidence for tuberculosis consisted of the epidemiologic evidence of exposure, the laboratory findings in the CSF and the clinical course. INH 20 mgm/kgm/day and rifampin<sup>8</sup> 20 mgm/kgm/day were begun and ampicillin was discontinued. A tuberculin skin test (intermediate strength) was placed on the patient. This was positive two days later, and with this the diagnosis of tuberculosis meningitis was accepted. Chloramphenicol was discontinued and streptomycin 20 mgm/kgm/day and hydrocortisone<sup>9</sup> 300 mgm/m<sup>2</sup>/day were added. Intrathecal medications were not used.<sup>10</sup> Cultures from the patient (CSF, bone marrow, gastric washings and urine) were negative for *Mycobacterium tuberculosis*. The chest Xray remained normal.<sup>11</sup> The brothers of the patient and his mother were begun on prophylaxis with INH and pyridoxine two weeks after the diagnosis was made in the patient. The father's treatment was begun a week later.

During the management of the patient, the following problems were encountered:

Seizures which began the first day in hospital and were controlled with phenobarbital and Dilantin.

Severe lethargy which progressed to coma lasting for approximately ten days.

Athetosis which increased until the third week and gradually resolved thereafter.

Hyponatremia was a persistent problem. The lowest serum sodium was 123 meq/1 on the third hospital day and gradually resolved during six weeks of hospitalization.

Elevated liver enzymes were noted on the 14th hospital day and resolved after INH was decreased to 10 mgm/kgm/day.

Nutrition was complicated by anorexia and by diarrhea producing a 20% weight loss. This problem gradually resolved without hyperalimentation.

A ventriculo-peritoneal shunt was placed for hydrocephalus after one month of hospitalization.

He was discharged on INH, rifampin and pyridoxine. At the time of discharge, he weighed 12.7 kgm. He had a partially resolved contracture of the left knee, and a resolving skin sluff of the dorsum of the left foot from an intravenous site that had infiltrated ten weeks earlier. This has not required grafting. He had deficits of speech and language and some unsteadiness of gait which have partially resolved at the time of this writing. Five months after his hospitalization began, he was able to pass the Denver Developmental Screen at his age level.

### Public Health Aspects

On the third hospital day, after the diagnosis of active tuberculosis was strongly suspected in the father of the patient, it seemed most undesirable that he circulate in the hospital or on the ward. On the other hand, the man's son was gravely ill. The result was that the father continued to visit until the sixth hospital day. The father was then asked not to visit until his own TB had been treated. The mechanics of documenting the father's illness and obtaining his medications took approximately three weeks.

### Epidemiologic Follow-up

Twenty-one hospital staff were identified with close patient contact. Four of the 21 were physicians working full time on the ward where the patient was treated. Three had responsibility for the patient's care. Consulting physicians and attending physicians were not thought to have had enough contact to require tuberculin skin testing. One non-physician moved out-of-state. Thus 20 staff including four physicians were available for testing. These people received three notices informing them that they should be tested. Eight weeks after the patient's admission, only ten of the 20 eligible staff and no physician had been tested. One physician reported for testing 12 weeks after the patient's admission. An additional effort to obtain testing was made by personally asking the untested contacts to report. Two months later, three physicians and one non-physician remained untested.

### Summary

A case of tuberculosis meningitis is reported which illustrates several important aspects of tuberculosis in children. The diagnosis was delayed and was aided by the family history. The illness was prolonged and severe including hyponatremia, seizures, coma, athetosis and hydrocephalus.

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- 6-11. Will be found on page 242.



# Emotional Impact of Diabetes Mellitus

GEORGE MAGNUS JOHNSON, M.D.\*

THERE IS LITTLE doubt in my mind that the emotional impact of diabetes mellitus, especially in adolescents, has as much potential for disabling a young person as does the disease itself.

Most of us probably treat diabetes adequately with insulin, but we often provide the young person with less than adequate understanding, direction, and guidance — especially during outpatient follow-up. The magnitude of the problem is illustrated by the fact that there are between 200 and 250 thousand adolescents with diabetes in the United States.<sup>10</sup> Recent studies in Michigan and Minnesota compute incidence at one in 550 school children.

What then should be our goal in helping establish a sound emotional milieu for the adolescent diabetic? According to Hofmann,<sup>13</sup> a logical management approach to the diabetic adolescent depends to a large degree on (1) compensation, (2) intellectualization, (3) displacement, and (4) constructive denial. But this approach also recognizes that destructive denial, regression, and projection do normally occur at various points in the course of the disease. Hofmann points out that the clinician's job is to "deter the damaging responses and promote felicitous approaches to the adolescent's growing need for independence, self-determination, and reassurance about body image integrity." He needs to be an active partner in his own care. I most heartily agree.

But what do studies say concerning the emotional status of insulin dependent diabetics? Surprisingly little is included in the pediatric literature, especially compared to the space given to the management of ketoacidosis.

Swift's much quoted 1967 study<sup>1</sup> found that diabetic children from various medical practices were more frequently diagnosed as having psychiatric disorders, notably anxiety and depression, than their non-diabetic peers. Sixty per cent of diabetics in the study received diagnoses compared to sixteen per cent of the control group. More recent studies have presented other findings.

Laron in Israel recently reviewed his twenty-year experience with 500 patients and noted that "good" control (by good control he means average blood sugar levels below 200, 24-hour glucosuria of 5 to 10 per cent, and normal plasma lipids) can only be achieved when the patient and his family have attained psychological stability.<sup>15</sup> This, according to Laron, may mean that effort be taken to reduce stressful situations influencing secretion of hormones affecting carbohydrate and fat metabolism such as catecholamines, growth hormone, cortisol and glucagon — all considered "stress" hormones.

In yet another study, Simonds<sup>3,4</sup> recently found that forty well controlled diabetic youths managed in the clinic of Jackson and Guthrie had fewer psychiatric diagnoses and interpersonal conflicts than both a non-diabetic study group and a poor control diabetic group.

Partridge<sup>11</sup> et al. found that teenagers with diabetes see themselves much the same as other adolescents concerning the important matters of freedom and responsibility in their daily lives. When their families were well educated they did not feel they were forced into responsibility for their own management too early. The youngsters felt, in terms of general understanding, that they *could assume responsibility by the age of 12 and complete management by age 15*. In my experience this has been entirely realistic.

Sullivan studied 12-16 year old diabetic girls using a self-esteem scale and a depression inventory.<sup>14</sup> Results were interpreted to mean that diabetic girls did not manifest deeper depression than non-diabetic girls, but rather they showed a greater awareness of their physiologic status. The importance of integrating adolescent developmental issues into treatment plans for diabetic patients was emphasized.

## Our Approach to Management

How can we achieve the goals promulgated by Hofmann and the apparent results summarized by Laron, Simonds and Partridge? Remembering the three stages of adolescence may help when we are beginning a diabetes education program.

1. Early (10-12)      The child is concerned about

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Given before the South Dakota Pediatric Society meeting, Rapid City, June 24, 1978.



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- real or imagined things such as threats to body image.
2. Mid (13-16) There is a struggle for autonomy and more concern about the opposite sex.
  3. Late (17-19) The young person becomes future oriented and ponders the effect of diabetes on career, marriage, longevity.

Like any other clinical group managing a number of diabetic adolescents, we have problems. In the strictest sense we are practicing preventive medicine. Prevention is the first and best cure for emotional ills in young diabetics. *Thorough initial and follow-up education, without finger wagging and threats is the key to prevention of emotional problems*, in my opinion. This takes time — lots of it. And even this highly individualized approach fails in some cases. For instance, I always feel a bit pessimistic when just one parent, the mother, is regularly present for initial education sessions.

Such was the case with 11-year-old John. John was a late child. His mother, despite thorough knowledge of diabetes, hasn't been able to accept the disease. John's dad, a hospital architect, was "too busy" to be present. John, therefore, has used the "crime-punishment" aspects of repetitive urine testing, diet management, and insulin administration to effectively manipulate everyone. His control is poor. There is really not much more the clinician can do.

Another point, on which there is some difference of opinion, is the nature of insulin therapy during the crucial first days and its effect on the eventual emotional status of teenagers and their parents. We agree with the use of intensive, high dose (four injections a day) regular insulin therapy for the first four to five days of treatment after diagnosis. This quickly establishes a so-called partial remission — negative urines, absence of hypoglycemia during the first weeks or months of diabetes and small insulin doses. This, in our judgment, provides a stable environment in which the child and his family can begin to learn to live with the disease.

Nothing is more upsetting to conscientious parents than a severe hypoglycemia episode shortly after their child has been discharged from the hospital. Miriam was a 12-year-old girl initially diagnosed and managed at a large diabetes clinic. Two weeks after she was discharged she had a severe reaction with seizures. She was on 20 units of Lente insulin. This so affected Miriam and her family that even mild hypoglycemia was hereafter avoided at all costs. Miriam's growth became stunted, puberty delayed, and Miriam used

her abundant cleverness to manipulate and dominate the family.

Avoidance of Somoygi effect is also essential for emotional stability in diabetes. We agree with Rosenbloom who recently suggested that this is the main reason for referral of adolescent insulin dependent diabetics 90 per cent of the time.<sup>6</sup>

Although the physician's time, education effort, and genuine personal interest are major items in preventing emotional problems in teenage diabetics several other points are worth consideration. Giving my home phone number to the family, particularly to the teenager, validates my interest and increases the chances that appointments will be kept.

One other factor, often underrated, which can be a source of emotional strength for teenage diabetics is exercise, the "invisible insulin." As much as anything I know, exercise meets Hofmann's goals of compensation and displacement. Ludvigsson in Linköping, Sweden, recently showed that teenage diabetics much preferred endurance exercise to doctor visits or meal plans.<sup>16</sup>

The "cure" of prevention, while ideal, is sometimes not possible to practice — especially when previously diagnosed and treated patients come to you, as mentioned in an earlier example. For these patients the services of a full-scale diabetes education center, such as Diabetes Detection and Education in Minneapolis or the Diabetes Education Center of Duluth, are available. We are now beginning to develop a similar center in North Dakota with branches in Fargo and Bismarck.

Although the question of emotional impact of diabetes is a complex one, we do know that parents can be helped to provide supportive, not intrusive, parenting. And though it takes time, it is essential to *like* the teenager, to show genuine interest in him/her, and to respect him/her. As Doctor Marble of the Joslin Clinic once said, "Love 'em, just a little bit."

Some of the findings of interested physicians and some of our own observations have been relayed, but because diabetes management is a family affair, it is appropriate to give you the views of a mother of diabetic children. They are in the form of a letter:

Dear Doctor:

You have diagnosed my child's diabetes. You have treated him efficiently and competently. But we both know this is just the beginning of what we hope will be a long course. Permit me a few observations now at the outset.

*On being normal.* Who is normal? Most of us decide for ourselves, based upon the messages society sends us, whether or not we are "normal." Occasionally we need to be reassured. Attitude surveys are good for that. But everyday habits are our prime indicators of



## EMOTIONAL IMPACT OF DIABETES MELLITUS — JOHNSON

how most of us decide we are normal. Don't, therefore, tell my child he is normal — "except for his diabetes." He knows very well he isn't. He has eyes. He has ears. He can reason. Alas, he is acutely, painfully aware of his differentness. In time he will come to define his own normality. Let him.

*On telling the truth.* My child needs all the resources he can garner to successfully control his destiny. The truth about what is expected of him, the reasons for making one choice over another, and the consequences of those choices is essential if he is to exercise responsibility and to enjoy the best of life. He deserves the truth.

*On delegating responsibility.* The sooner you and I begin to show my child that he can make good, informed decisions which result in his well-being, the sooner he begins his life-long program of self-care, the more independent, confident, and well-adjusted he will be. Don't let me coddle him and make excuses for him. Above all, don't make him a captive of someone else — neither of you nor of me.

Dear doctor, thank you for listening — thank you for your share of our mutual trust.

A mother

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# Laboratory Letter

## Hypothesis to Explain the Emergence of Early Onset Group B Streptococcal Infection in Newborns

RALPH A. FRANCIOSI, M.D.\*

The incidence of early onset GBS infection has increased in the United States over the past decade. This has paralleled the increased incidence of maternal vaginal colonization. The hypothesis presented is that increased maternal vaginal colonization with GBS is explained by obstetrical practices that stress evaluation of the course of labor and delivery. If this hypothesis is valid then reduction of the quantity of maternal vaginal GBS will decrease the incidence of early onset GBS infection.

FOLLOWING OUR initial observations on Group B streptococcal (GBS) infection,<sup>1,2</sup> we have observed this disease emerge over the past decade to become the leading cause of early onset bacterial infection (infection <48 hours following birth). The incidence, in the United States, is approximately 8,000 cases per year with a mortality of 4,800.<sup>3</sup> This paper will address the question why there has been a significant increase in early onset GBS infection.

Identification of GBS was established by Lancefield in 1933.<sup>4</sup> Although bacteriologists were capable of identifying GBS, no increase in early onset GBS infection was reported prior to 1961.<sup>5</sup> The clinical incidence of neonatal bacterial infection remains at approximately 5/1000 live births, however, the frequency of gram negative infections has decreased as GBS increases.<sup>6</sup> Since the mortality of early onset GBS infection is approximately 60% and the clinical presentation mimics hyaline membrane disease, lack of recognition at autopsy could account for the decreased incidence prior to 1969. However, the discipline of pediatric pathology has been practiced in most large pediatric units since 1940 and any significant increase in congenital bacterial pneumonia would have been detected.

Table 1 documents the increased colonization of maternal vagina at delivery from 1934-1977. Table 2 shows that with the use of selective media the incidence of maternal vaginal colonization increased. Table 3 lists the adult reservoirs of GBS and the higher percentages were detected by selective media. Attention is called to the frequency of vaginal and anal colonization in pregnant and non-pregnant women and

in males and females attending venereal disease clinics. These studies support the hypothesis<sup>15,16</sup> that the origin of vaginal GBS is anal flora.

The risk of newborn colonization with GBS in vaginally positive women varies from 26% to 39% in studies using non-selective media and 41% to 98% when selective media is used. The risk of developing early onset GBS infection in colonized newborns

TABLE 1 Isolation of Maternal Vagina GBS by Non-selective Media			
	Ref.	# Cases	+ GBS (%)
Hare <sup>7</sup>	1934	885	1.4
Lancefield <sup>8</sup>	1935	—	2.3
Kexel <sup>9</sup>	1965	—	9.5
Hood <sup>5</sup>	1961	208	5.2
Franciosi <sup>2</sup>	1973	977	4.6
Reid <sup>10</sup>	1975	369	4.9
Mhalu <sup>11</sup>	1977	125	8.8

TABLE 2 Isolation of Maternal Vagina GBS by Selective Media			
	Ref.	# Cases	+ GBS (%)
Baker <sup>12</sup>	1973	205	22.5
Aber <sup>13</sup>	1976	297	21.5
Finch <sup>14</sup>	1977	110	6.4
Badri <sup>16</sup>	1977	789	10.2
Mhalu <sup>11</sup>	1977	125	14.4
Ferrieri <sup>17</sup>	1977	759	8.3
Anthony <sup>18</sup>	1978	320	12.8
Duben <sup>19</sup>	1978	464	4.5

TABLE 3 Adult Reservoirs of GBS (%)				
	Vagina	Anus	Urethra	Throat
Non Pregnant	5.7-14.7	8.4-?	18.7-27.3	3.9-5.0
Pregnant	11.3-18	3.7-14.6	?	1.0-?
Female V.D.	?-28.5	—	—	—
Male	—	—	3.8-?	—
Male V.D.	—	—	19-?	—

\*Director of Pathology at Children's Health Center and Hospital, Minneapolis, Minnesota.



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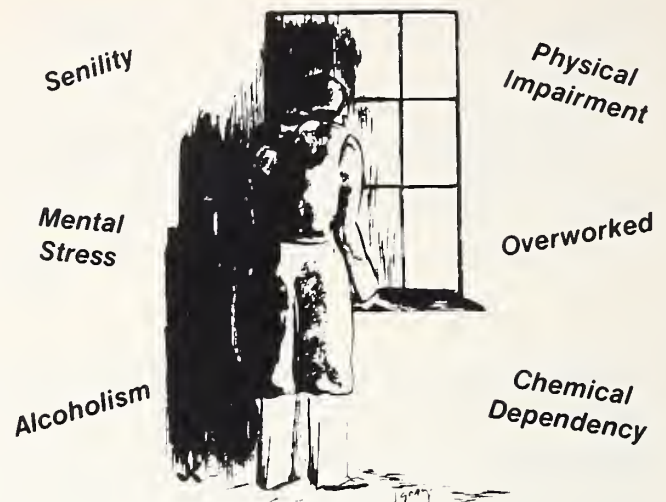
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varies from 14% to 25% when non-selective media is used and 1.3% to 14% with selective media. The correlation of early onset GBS infection, newborn colonization and maternal vaginal colonization is more accurate when non-selective media is used. This indicates that although selective media is more accurate in defining the presence of GBS it is less accurate in predicting the risk of early onset GBS infection.<sup>20</sup> I interpret these observations as support for the hypothesis that the quantity of maternal vaginal GBS is directly proportional to the incidence of early onset GBS infection.

During the past decade there has been a radical change in obstetrical management of pregnant women and their offspring. Labor and delivery have been closely monitored in order to evaluate the progress of labor and detect fetal hypoxia. The methods of evaluation range from frequent rectal and/or vaginal

examinations to internal fetal monitoring.<sup>21</sup> My hypothesis is that the increase in maternal vaginal GBS is related to these procedures. Support for this hypothesis comes from a review of 320 cases of early onset GBS<sup>22</sup> which recorded that most infants were premature (79%) and hypoxic (78%). Since prematurity and fetal hypoxia are major risk conditions, the probability exists that these deliveries were frequently monitored. Additional support is the study of Yow<sup>23</sup> showing that transmission of GBS to newborns from maternal vaginal flora is reduced by treatment with Ampicillin intrapartum. Presumably this antibiotic treatment reduced the quantity of maternal vaginal GBS. I would argue then that reduction in the incidence of early onset GBS infection can be accomplished by reducing the quantity of GBS in maternal vagina.

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# Case Report

## Femoral Tuberculous Arteritis

LAWRENCE N. MULMED, M.D.\*; DAVID N. WILLIAMS, M.B., Ch. B., MRCP (UK)†; MICHAEL W. CHOPEK, M.D.‡  
and DEMETRE N. NICOLOFF, M.D.‡

**A case of tuberculous pseudoaneurysm of the femoral artery is presented. Previous reports are reviewed and tuberculosis of the arterial system is discussed.**

ALTHOUGH TUBERCULOUS obliterative endarteritis of small arteries is frequently seen in areas of active infection,<sup>1,2</sup> vascular involvement elsewhere is unusual. Tuberculosis of the aorta has been reported in more than 100 patients,<sup>1-6</sup> usually secondary to direct extension from tuberculous adenitis or abscess. Tuberculosis of the femoral artery is rare; only seven cases have been documented previously, and six of these presented with aneurysms. This report describes a patient with sudden onset of a tuberculous femoral aneurysm who subsequently died of miliary tuberculosis. Previous reports of this entity are reviewed, and tuberculous involvement of the vascular system is discussed.

### Case Report

A 67-year-old white man was admitted to the University of Minnesota Hospitals complaining of tenderness, pain, and swelling in the left groin and pain in the left lower extremity of three days' duration. The patient had spent the previous three months in Arizona. He had had a dry cough for a few days and later admitted to anorexia, easy sweating, and an eight pound weight loss over the preceding month. There was a questionable history of positive tuberculin skin test. In 1972, an atherosclerotic abdominal aortic aneurysm had been resected with insertion of a synthetic Dacron bifurcation graft. He was taking alpha-methyldopa and hydrochlorothiazide for hypertension.

On admission his temperature was 100° F, blood pressure 140/70 mm Hg, and pulse 120/min. Lung fields were clear to auscultation. A red, tender pulsatile mass was present in the left groin. The left leg was cool but viable. The popliteal, dorsalis pedis, and posterior tibial pulses were not palpable in the left leg and were diminished in the right. Hemoglobin was 13.8 gm and the white blood cell count was 8,000 cells/cu mm with 74 percent neutrophils, 17 percent lymphocytes, and 9 percent monocytes. The serum sodium was 129 mEq/L, potassium 3.7 mEq/L, chloride 92 mEq/L, bicarbonate 29 mEq/L, blood urea nitrogen (BUN) 14 mg percent, and creatinine 1 mg percent. Serum glutamic-oxaloacetic transaminase (SGOT), alkaline phosphatase, and glucose were normal. Chest roentgenogram showed mild bilateral interstitial changes, discoid atelectasis in

the right upper lung field, normal heart size, and an ectatic aorta with calcium in the wall (Figure 1).

Translumbar aortography showed a widely patent graft, atherosclerotic changes of both distal iliacs and hypogastric arteries, and occlusion of the right superficial femoral artery with multiple collaterals (Figure 2). There was gradual fading of contrast in the left femoral artery suggestive of an extrinsic defect. The left superficial femoral artery was not visualized, but there was opacification of the profunda via collaterals. A mycotic aneurysm was suspected, blood cultures were obtained, and treatment with intravenous cephalothin was begun.

During the next 12 hours the groin pain increased and the mass enlarged. At surgery, a pseudoaneurysm secondary to rupture of the common femoral artery was found and excised. No direct contiguity was found between the aneurysm and the Dacron prosthesis. Because of presumptive infection and the fact that the left leg seemed viable, no replacement of the involved segment of artery was attempted. Portions of the pseudoaneurysm were sent for routine culture and histology.

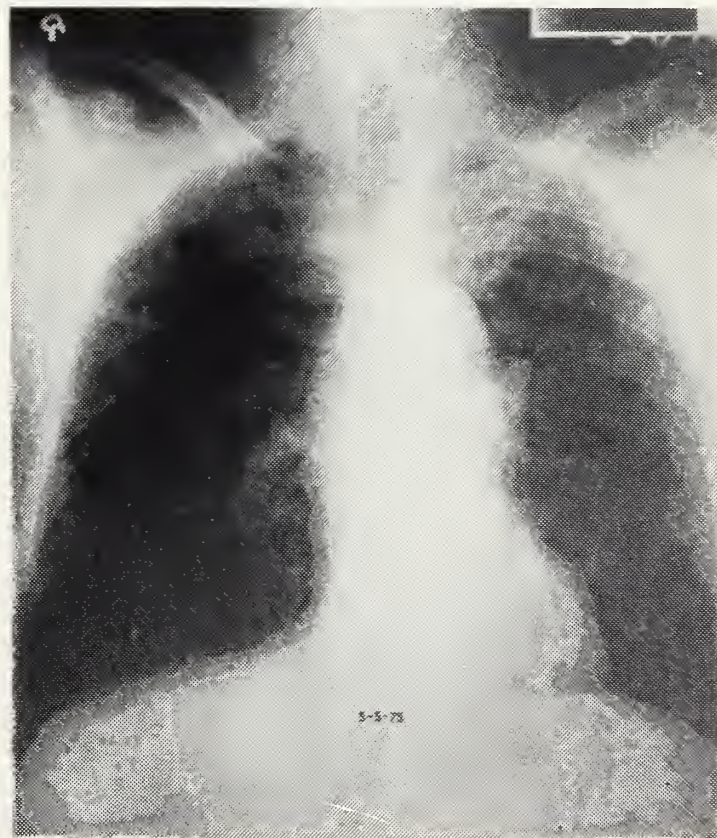


Fig. 1 — Chest roentgenogram obtained on admission shows mild bilateral interstitial changes and discoid atelectasis in the right upper lung field.

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Microscopic examination of the resected portions of the aneurysm showed moderate atherosclerosis with hyalinized thrombus and necrotizing arteritis. Marked intimal destruction and replacement by necrotic material was seen extending into and focally through the media (Figure 3). The remaining portions of media and adventitia showed infiltration with lymphocytes, histiocytes, Langhans' type giant cells, and granulomas with central necrosis (Figure 4). Surrounding the resected aneurysm there was dense fibrous and granulation tissue, as well as frequent obliterative endarteritis of smaller vessels. Stains for acid-fast bacilli, fungi, and bacteria were negative.

Postoperatively, his temperature rose to 104°F in spite of sequential trials of cephalothin plus gentamicin and of chloramphenicol. Multiple blood cultures for aerobic and anaerobic bacteria and fungi yielded no growth. Sputum smears for acid-fast bacilli; skin tests for purified protein derivative (PPD-S), streptokinase — streptodornase (SKSD), coccidioidomycosis, and histoplasmosis; and serum studies for histoplasmosis, blastomycosis, coccidioidomycosis, and febrile agglutinins were negative. Serum protein values and immunoelectrophoresis were normal. Upper GI series, barium enema, intravenous pyelogram, proctoscopic examination, lumbar puncture, and brain, lung, and liver scans failed to reveal a focus of infection. Bone marrow biopsy showed numerous granulomas with giant cells and early necrosis, but all special stains were negative.

On the seventeenth hospital day, progression of the pulmonic interstitial infiltrate was evident and empirical antituberculosis therapy with isoniazid, rifampin, and ethambutol was begun. Fever continued.

On the twenty-fourth hospital day the patient underwent open-lung biopsy and closed liver biopsy because of the lack of diagnosis and the possibility of fungal or tuberculous infection. At surgery, multiple nodules were palpable in the lingular segment, and biopsies were taken. Postoperatively, a 1500-cc blood loss occurred through the chest tube. Re-exploration revealed oozing from the intercostal muscle bundle, which was cauterized. However, the patient became hypotensive and severely acidotic (pH 6.9) and died four hours later despite intensive intravenous therapy with bicarbonate, cephalothin, methyl-prednisolone and fresh blood.

At autopsy, disseminated granulomas were found in the lungs, liver, spleen, kidneys, adrenals, lymph nodes, and prostate, in addition to the left femoral artery and bone marrow lesions previously described. Acid-fast bacilli were seen in most of these organs and were also found on resectioning the femoral aneurysm (Figure 3). No lymphadenopathy was evident in the area of the femoral aneurysm. The abdominal aortic graft was surrounded by dense fibrous tissue without inflammation, and acid-fast stains from several areas of the graft were negative. Cultures of tissue from lung, liver, and bone marrow were positive for *Mycobacterium tuberculosis*. Tissue from the aortic aneurysm resected in 1972 was reviewed and showed an atherosclerotic aneurysm with minimal lymphocytic infiltrate. Multiple sections of this tissue were also negative for acid-fast bacilli.

### Previous Cases of Femoral Artery Tuberculosis

Of the seven patients previously reported as having tuberculosis involving the femoral artery, four died from complications of the underlying disease.<sup>6-12</sup>

Pertinent information about these and the present case are reviewed in the Table. Of interest is the relative

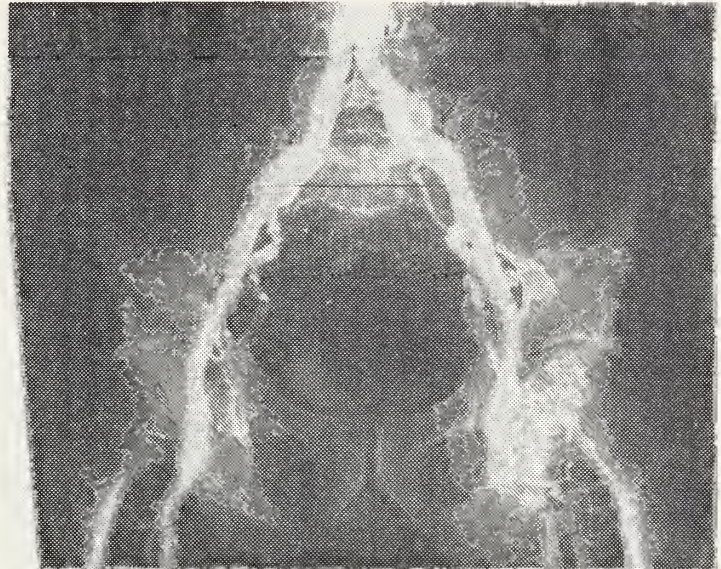


Fig. 2 — Translumbar aortogram shows the aortic bifurcation graft and occlusion of the left femoral artery. The left superficial femoral artery is not visualized, but there is opacification of the profunda via collaterals. The right superficial femoral artery is occluded.

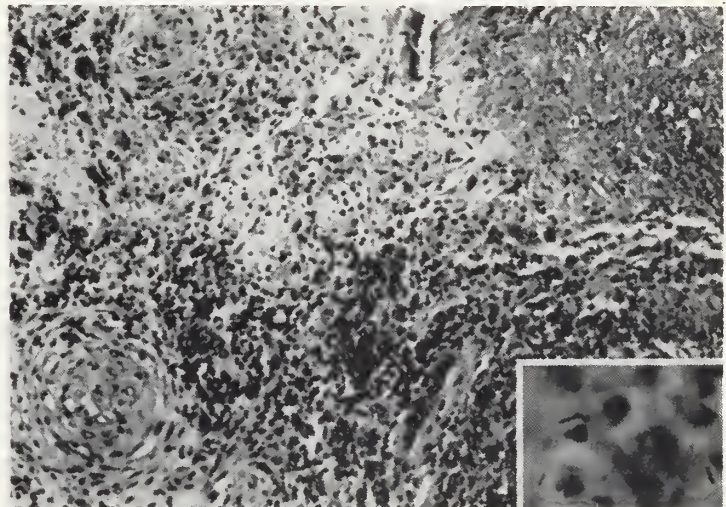


Fig. 3 — Necrotizing arteritis from resected femoral aneurysm. Although not seen on original section (see text), the focus of necrosis (right upper corner), primarily on the luminal surface, contains many acid-fast bacilli (insert). In addition there is chronic inflammation and obliterative endarteritis (H & E x 100; insert Ziehl-Neelson x 1600).

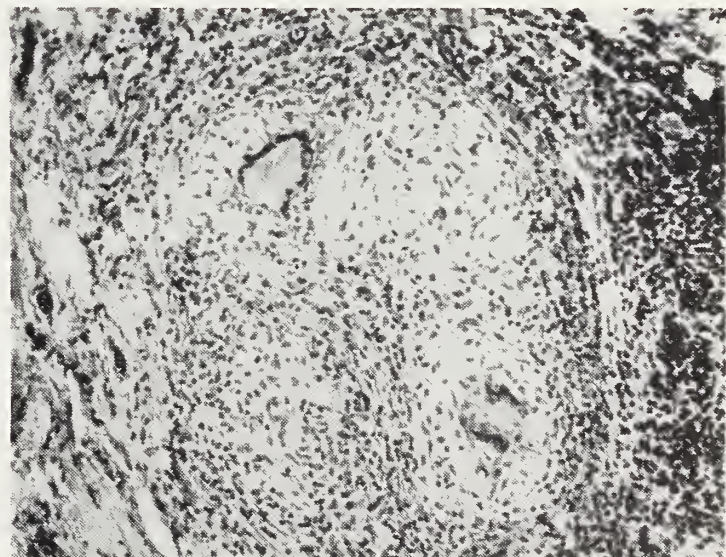


Fig. 4 — Granulomatous inflammation on adventitia of resected aneurysm, with two Langhans' type giant cells (H & E, x 100).



frequency of involvement of the artery by way of the vasa vasorum, effectively isolating the tuberculous arterial focus from tuberculosis elsewhere. Smith et al<sup>11</sup> emphasized lymphatic spread to the artery without node involvement. Jepson and Meadows<sup>12</sup> noted at autopsy of their patient that the tuberculous lesion in the artery appeared to be of much longer duration than the generalized miliary foci elsewhere. This led them to speculate that the arterial lesion could have been responsible for miliary spread.

### Discussion

Tuberculosis of the aorta has been reported in more than 100 patients since Weigert's<sup>13</sup> initial report. Three mechanisms of involvement have been proposed:<sup>14</sup>

- (a) Direct hematogenous implantation on the internal surface where slight injury or other change

has occurred, as with an atheromatous ulcer.

- (b) Transportation of the organism to the adventitia or media by the vasa vasorum.

- (c) Direct extension from tuberculous lymph nodes or abscess.

The last mechanism seems to be the most common and often results in formation of false aneurysm.<sup>6</sup> In addition, direct extension has occurred from empyema, spondylitis, or paravertebral abscess.<sup>5</sup>

The same mechanisms seem to apply to femoral artery involvement. However, in contrast to the aorta, the femoral artery is more typically involved via the vasa vasorum. In addition, transportation of the organism by way of lymphatic channels also has been described.<sup>11</sup> In our patient, no evidence of local lymph node involvement or dilatation of the lymphatics was noted. Thus, seeding of an atherosclerotic area with subsequent intimal disruption or involvement by way

TABLE  
Cases of Femoral Artery Tuberculosis Reported in the Literature

Author & Year	Sex & Age	Aneurysm Site & Type	Histology	AFB Seen	Tbc Culture	Duration & Nature of Illness
Geissler <sup>7</sup> 1906	M 52	None. Tubercles on intima of femoral artery	Granulomas	Yes	No	Symptoms of lung disease.
Brockman <sup>8</sup> 1926	M 14	Ruptured R common femoral	All arterial layers showed giant cells, endothelial cells & caseation.	No	No comment	12 days. Ache & stiffness in R thigh. Acute R groin pain after 12 days.
Malcolm <sup>9</sup> 1928	M 78	Ruptured R femoral aneurysm	Diffuse necrosis, giant cells, fibrous proliferation.	Yes	No comment	6 days pain R knee & thigh. Subsequently became listless, & developed pneumonia.
Baumgarten <sup>10</sup> 1933	M 53	Ruptured L femoral aneurysm mid 1/3 of thigh.	Caseating tubercles with giant cells, most abundant in media. Periostitis.	Not done	No comment	2 yrs previously pt. had 2 wks of pain inner L thigh. Painful swelling developed in same region 3 wks before admission.
Smith <sup>11</sup> 1957	M 78	Ruptured saccular aneurysm L superficial femoral artery (junction of mid & lower 1/3).	Fibrin filled sac. Areas of proliferation & caseation. Evidence of local lymphatic spread.	Yes	No comment	5 yrs previously Tbc of R femur with midthigh amputation. Rx with PAS & streptomycin. 12 mo. later Tbc of L ankle & prepatellar bursa. Same drugs repeated. 6 mo. later aneurysm developed.
Jepson <sup>12</sup> 1962	F 78	False L femoral & popliteal aneurysm.	Caseation & Tbc granulation tissue.	Yes	No comment	Admitted with 3 wks painful swelling behind left knee. Downhill febrile illness over next 7 wks.
Volini <sup>6</sup> 1962	M 59	a) 1959: Tbc aneurysm of abdominal aorta. Many local nodes. b) 1961: L femoral artery aneurysm at level of femoral canal. No local nodes.	Epithelioid & giant cell tubercles and areas of caseation. Epithelioid & giant cell tubercles and areas of caseation.	Yes No	Yes Negative	R UL lesion on CXR for 6 yrs. Abdominal pain 1959, Tbc aneurysm resected, Teflon graft replacement, chemotherapy started. 18 mo. later developed fever followed by pain in L thigh.
Mulmed (current)	M 67	Pseudoaneurysm of L common femoral artery.	Langhans giant cells, granulomas with central necrosis, necrotizing arteritis, obliteration of small vessels.	Yes	Yes From other tissues (see text)	One month weight loss & anorexia. Cough for 1 wk. Pain in groin & leg for three days.



of the vasa vasorum may have occurred.

Recent review articles on miliary tuberculosis<sup>15,16</sup> or mycotic aneurysms,<sup>17,19</sup> and standard textbook descriptions of these disorders<sup>20-22</sup> make little or no mention of tuberculous arteritis. Reports of tuberculous involvement of other arteries also are rare. Liebermeister<sup>23</sup> noted two cases of radial artery tuberculosis and stated that tuberculosis of small arteries of the extremities was relatively frequent. Other reports include tuberculous involvement of the hepatic,<sup>24</sup> iliac,<sup>3,25</sup> and coronary arteries,<sup>26</sup> as well as the carotid artery.<sup>11</sup>

Several features of the course of events in our patient deserve comment. A femoral mycotic aneurysm secondary to tuberculosis is extremely unusual, since most mycotic aneurysm are bacterial in origin.<sup>17,19</sup> The granuloma seen on histologic examination of the aneurysm plus a changing chest xray prompted us to add tuberculosis and fungal disease to the differential diagnosis. The patient's recent trip to Arizona raised the question of disseminated coccidioidomycosis, although we were unable to find any reports of

aneurysm secondary to this organism.

Death was caused by a combination of factors, including shock and acidosis. The possibility of adrenal insufficiency also existed in view of terminal hypotension and moderate tuberculous involvement of the adrenals. In this regard, the patient had been mildly hyponatremic during his illness, although potassium values were normal. Blood pressure likewise was normal until the final hours, inspite of a history of hypertension.

### Summary

Tuberculosis rarely involves major arteries. Mechanisms by which tubercle bacilli invade the vascular tree could include: direct hematogenous implantation on the internal surface, spread by way of the vasa vasorum or lymphatics, or direct extension from tuberculous lymph nodes or abscesses.

Of the more than 100 reported cases of tuberculosis of the aorta, only seven have involved the femoral artery. We report a 67-year-old white man who presented with a pseudoaneurysm of the left femoral

TABLE (Continued)

Author & Year	Signs of Aneurysm	Tuberculosis Elsewhere	Proposed Pathogenesis	Treatment	Outcome
Geissler <sup>7</sup> 1906		Diffuse miliary Tbc; Tubercles on intima of aortic and iliac arteries.	Via blood stream.	—	Died.
Brockman <sup>8</sup> 1926	Swelling, pulsation, bruit over femoral artery.	Tbc of spine 2 yrs. previously.	Via vasa vasorum.	Excision and ligation	Breakdown of incision & overlying skin with subsequent healing.
Malcolm <sup>9</sup> 1928	Swollen R leg. Mass in upper 1/3 of thigh with bruit. Ecchymoses inner thigh.	At autopsy — diffuse miliary Tbc.	Vasa vasorum.	None	Death due to miliary Tbc 23 days after knee pain began.
Baumgarten <sup>10</sup> 1933	Lobular swelling inner L thigh. No systemic signs.	None.	Via vasa vasorum into media.	Exploration of area without finding aneurysm. Rebled. Amputation on 27th day.	3 yrs. later patient was doing well.
Smith <sup>11</sup> 1957	Cyanotic cold L foot. Pulsatile mass, junction mid & lower 1/3 of artery.	Previously in R femur, L ankle and L pre-patellar bursa.	Via lymphatics from synovium of ankle & pre-patellar bursa.	Aneurysmectomy & patency of vessel restored. INH, PAS, streptomycin for 30 days.	Good vascular flow. Died of myocardial infarction 6 mo. later. Artery and remained patent.
Jepson <sup>12</sup> 1962	Palpable, pulsatile tender mass inner side of L popliteal fossa.	Miliary Tbc. at post mortem. Undiagnosed during life.	No comment.	Lumbar sympathectomy & ligation of femoral artery at adductor opening.	Death due to miliary Tbc.
Volini <sup>6</sup> 1962	Palpable mass L lower thigh. Absent pulses in foot.	Aorta. Fistula between aorta and small bowel appearing after femoral aneurysm.	a) Local lymph node spread to aorta.  b) To femoral artery via blood stream.	Excision of femoral aneurysm and chemotherapy.	Death due to massive hematemesis. No autopsy.
Mulmed (current)	Red, tender pulsatile mass in groin.	At autopsy, diffuse miliary Tbc.	Seeding of atherosclerotic area or via vasa vasorum.	Excision of aneurysm and chemotherapy.	Death due to shock, acidosis, and miliary Tbc.



artery associated with fever. His illness remained undiagnosed in spite of surgical extirpation of the aneurysm, treatment with various antibiotics, and exhaustive investigations. At autopsy he was found to have miliary tuberculosis. Resectioning of the aneurysm revealed acid-fast bacilli. Implications of this case are discussed and compared with others from

the literature.

#### Acknowledgments

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# Inflammatory Diseases

## Polymyositis with Pulmonary Infiltrate and Pleural Effusion

DONALD G. ROACH, M.D.\* and WILSON M. SALTER, M.D.†

**Polymyositis-dermatomyositis in association with primary pulmonary disease is not common. A careful search for occult muscle disease in patients with muscle weakness and pulmonary disease is important. An unusual presentation is described and then discussed with reference to previously reported cases. Treatment of Polymyositis-dermatomyositis is yet somewhat uncertain. Some patients have shown good response with Prednisone therapy.**

**P**OLYMYOSITIS AND dermatomyositis are uncommon inflammatory diseases known to affect skin, striated muscle, and connective tissue. Although involvement of lungs and/or pleura has been commonly described in other connective tissue diseases, primary pulmonary disease in association with polymyositis-dermatomyositis (PM-DM) was not described until Mills and Mathews in 1956 reported a patient with DM whose presenting symptoms were cough and dyspnea. The chest radiograph demonstrated increased interstitial pattern and interstitial fibrosis with chronic round cell infiltration of the alveolar walls demonstrated at autopsy. Schwartz, et al.<sup>4</sup> report that between 1956 and 1976 only 37 cases of primary pulmonary diseases in association with PM-DM have been well documented and well described.

We report a patient who was referred to us with complaints of fever of unknown origin of three weeks duration. Additional presenting symptoms included dyspnea, cough, weakness and anorexia. Accompanying chest roentgenograms were felt to be consistent with a left lower lobe pneumonitis. Further studies included an Abram's pleural biopsy which revealed acute degenerative myositis consistent with polymyositis. The patient has shown significant clinical improvement following treatment with high dose Prednisone.

### Case Report

This is a 67-year-old white female part-time teacher and housewife with a complaint of fever of unknown origin and a left lower lobe pneumonitis. She first became ill three weeks prior to being admitted to this hospital, when she developed a fever and cough. Antibiotics were begun which did relieve her symptoms for a

period of three to four days; however, recurrent fever as well as chills, anorexia, and progressive weakness of all musculature appeared. The patient was hospitalized for one week and then transferred to this hospital because of no clinical improvement, and continued pulmonary infiltrate as well as a new left pleural effusion after intravenous antibiotic therapy (Figure 1).

The patient reports that she had otherwise been in good health until this acute illness. She does admit to a non-productive cough although denies hemoptysis. She did experience dyspnea, marked weakness and anorexia, but no significant chest pain. Urinary tract symptoms were denied. There has been no diarrhea or constipation and no melena. She denied headache, dizziness, or visual disturbances. Her past history revealed no significant diseases or illnesses except for one episode of pneumonia ten years earlier. Heart disease, rheumatic fever, heart murmur, hypertension, renal diseases, diabetes mellitus and tuberculosis were all denied. The patient had had no previous surgery. Her health habit history was negative for tobacco and alcohol uses.

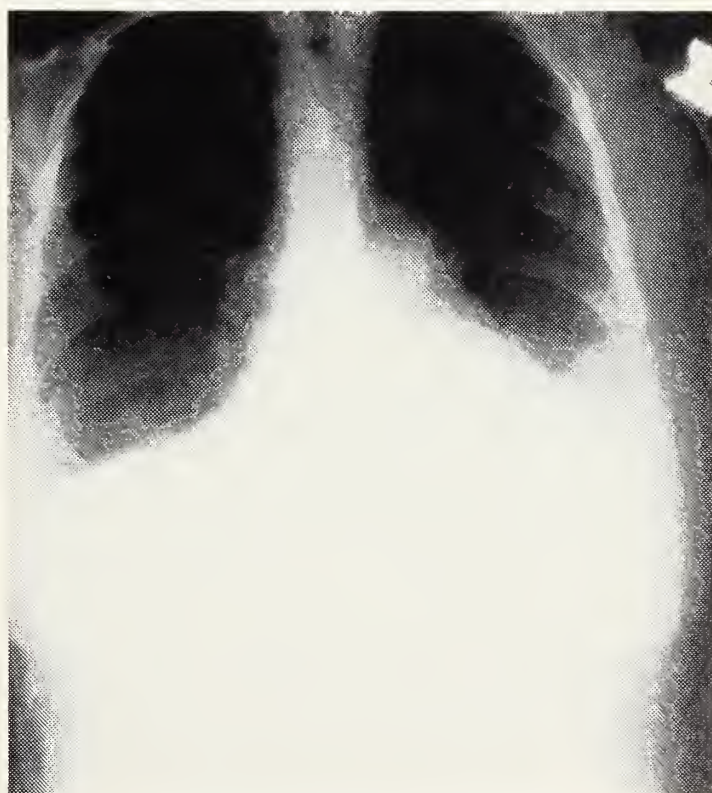


Fig. 1 — Admission chest radiograph.

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Examination at the time of admission revealed an alert and well nourished female who was weak and unable to move from the supine to sitting position without help. Vital signs: Blood pressure 130/50, pulse 100, respirations 24, temperature 101° F (0). Abnormal physical findings included diminished breath sounds bilaterally with inspiratory rales at the left base. There were no rhonchi. Lower extremity exam revealed a trace of pitting edema bilaterally. Musculoskeletal exam demonstrated no muscle tenderness to palpation and extremity muscle strength including proximal muscle groups was normal. She did have abdominal muscle strength weakness with an inability to raise to a sitting position from the supine without assistance. No skin rash was observed.

The patient remained febrile throughout the first week of hospital investigation. Admission hemoglobin was 14.3, WBC 22,800 with a marked left shift. Erythrocyte sedimentation rate was 36 mms./hour. Admission chest roentgenogram demonstrated pleural reaction and parenchymal infiltrate at the left lung base. The right lung was clear. Multiple sputums for gram stain and cultures were negative. Acid fast sputum smears and cultures were negative. Blood cultures were sterile.

Serum complement fixation titers for histoplasmosis, blastomycosis, and the actinomyces and micropolyspore organisms were all negative. Serum enzyme studies revealed a markedly elevated creatine phosphokinase at 3880 (normal 50-160 IU/L). SGOT and LDH were moderately elevated at 149 (normal 8-33 IU/L) and 711 (normal 100-190 IU/L) respectively. BUN, calcium, phosphorus, creatinine, and electrolytes were all normal. Serum hepatitis B antigen was negative and serum hypersensitivity pneumonitis serologies were negative. An L. E. preparation, rheumatoid factor, FANA, tuberculin skin test, and cold agglutinins titer were all negative. An electrocardiogram demonstrated possible residual of an old anteroseptal myocardial infarction but was not otherwise outside normal limits. Fiberoptic bronchoscopy was performed and was entirely normal. A lung scan revealed only decreased uptake at the bases as would be expected with a pleural reaction or pneumonitis. Pulmonary function studies were attempted but the patient was too

weak to give valid results.

A repeat chest film on the third hospital day showed some slight clearing of the infiltrate; however, free fluid was now evident at the left lung base.

Fever was yet present on the seventh hospital day. Because of the continued elevated temperature and left pleural effusion, an Abram's pleural biopsy and pleural aspiration thoracentesis were performed.

The biopsy revealed skeletal muscle tissue with patchy foci of basophilic degeneration with loss of cross striations and enlargement of nuclei that was associated with an accompanying mononuclear cell inflammatory process. No definite arteritis was identifiable. There was no evidence of muscle regeneration. These findings were interpreted as indicating an acute degenerative myositis consistent with polymyositis. Stains and cultures of aspirate were negative for acid fast and fungal organisms. Aerobic and anaerobic cultures were also negative.

Clinical and laboratory findings were felt to be consistent with a pathological diagnosis of polymyositis and the patient was begun on Prednisone 20 mg. t.i.d.

On the ninth hospital day the patient's course was complicated by an episode of acute arterial occlusion involving right and left femoral arteries. A bilateral femoral arteriotomy procedure with embolectomy from the right iliac and right popliteal region, also left iliac and left distal femoral tree, was performed. The patient was maintained on Heparin and then converted to an oral anticoagulant.

Marked improvement with lysis of fever, improvement in over-all weakness as well as a slow improvement in the dyspnea was noted following the start of oral Prednisone therapy.

**TABLE**  
**CPK Enzyme Determination throughout Hospital Course**

	Hospital Day	CPK
	2	4040
	3	3880
April 3, 1978 — Day 6	5	3520
Prednisone therapy started→	9	2140
	13	1143
	16	840
	19	1024
	23	476
	26	480
Days Post Discharge	17	65

Serial CPK enzyme determinations throughout the patient's hospitalization are thought to demonstrate improvement in muscle disease.

The patient was discharged on the twenty-seventh hospital day to remain on Prednisone 20 mg. q.a.m. and was followed in clinic one, three and five weeks after discharge. She has shown continued improvement with increased strength, less cough and dyspnea. Chest roentgenograms continue to show improvement and a tapering of the corticosteroid regimen has reduced the daily Prednisone dosage to 30 mg. The patient will, of course, continue to be followed closely in the clinic, monitoring the course of her polymyositis as well as following her closely for the development of a malignancy. (Ten percent of all adults, especially the elderly, who have PM-DM are found to have a carcinoma or some other tumor.)<sup>5</sup>

## Discussion

Primary pulmonary disease in association with



Fig. 2 — Day 10 of prednisone therapy.



PM-DM was not recognized prior to 1956 and since that time only 37 well documented cases have been described in literature. Hepper, in the *Medical Clinics of North America*, 1964, proposed three mechanisms for the development of pulmonary disease in the patient with PM-DM: (1) Aspiration pneumonia; (2) Hypoventilation with a secondary hypostatic pneumonia; and (3) A primary form of interstitial pneumonia.<sup>4</sup> The first two mechanisms are not specific for PM-DM but are possible in any chronic neuromuscular disorder with involvement of the respiratory musculature. Methotrexate which just recently has been included in the treatment of certain cases of PM-DM has been implicated in the development of a pneumonitis that occurs with its prolonged use so that drug related lung disease may also soon become an important etiologic agent in the development of pulmonary disease with PM-DM.<sup>4</sup>

The patient presented here was referred to us with a diagnosis of a fever of unknown origin; however, her chief symptoms were dyspnea and a non-productive cough, which, after having reviewed the 37 well documented cases reported to this date, are the two most common presenting symptoms of PM-DM with associated pulmonary disease. Schwartz, et al. in reviewing the literature reports that 68% of these patients were females with an average age of 50 years. Also, in slightly less than half of these cases, muscle and/or skin complaints were preceded or masked by pulmonary symptoms by as much as three years.<sup>4</sup>

Interpretation of the initial chest roentgenogram in

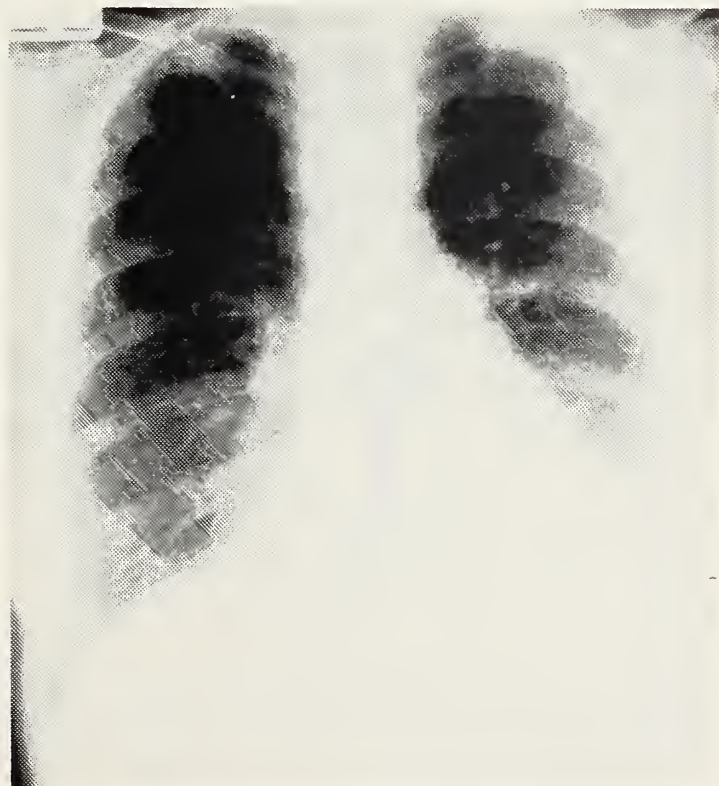


Fig. 3 — Five weeks of Prednisone therapy.

this case identified a pleural reaction and parenchymal infiltrate at the left lung base. Radiographs usually demonstrate diffuse linear interstitial lung infiltrates with predilection for the lower lung zone.<sup>4</sup> Accentuated linear markings at the bases are common early findings with the development of patchy consolidation, nodulation, honeycombing and evidence of pulmonary hypertension and cor pulmonale appearing later.<sup>2</sup> Pleural reactions on the radiograph have not been reported prior to 1976; however, Schwartz and his colleagues, although not able to demonstrate radiologic evidence of pleural involvement, were able to histologically confirm evidence of pleural involvement in 50% of their cases.<sup>4</sup> Chest film changes of mixed alveolar and interstitial infiltrates have been described in ten of the previously reported cases prior to Schwartz's work. The Schwartz study suggests an early stage of primary PM-DM pulmonary disease consisting of organizing pneumonitis and bronchiolitis as well as non-specific interstitial pneumonitis to account for this radiographic pattern. He and his associates would suggest that this pulmonary inflammation later progresses to an interstitial fibrosis pattern.<sup>4</sup> Duncan, et al. 1974, recognizes two general types of pulmonary diseases in association with PM-DM and ascribes prognostic significance to these types.<sup>1</sup>

In one there is a chronic progressive course; histologically, pulmonary fibrosis is predominant. These patients show poor response to steroids with regard to improvement in the pulmonary disease. In the second type, patients run a more acute course with histologic alveolar wall thickening, distortion, and acute inflammatory infiltration, while at the same time there is little fibrosis evident. These patients show good response to steroid therapy.<sup>1</sup> Schwartz, et al, report after examining 28 patients on whom information was available, that the presence of active inflammation on lung biopsy is a predictor of good therapeutic response.<sup>4</sup>

At the present time there appears to be little means of predicting which patients with PM-DM will develop pneumonitis. No relationship to severity or duration of disease can be demonstrated and positive serology tests and muscle enzyme elevations seem to have likewise little bearing. The presence or absence of skin lesions has not been demonstrated to alter the prognosis.<sup>3</sup>

Previously reported cases of PM-DM with associated pulmonary disease commonly demonstrate elevated sedimentation rates and tests for rheumatoid factor are usually positive. The FANA is usually negative while the CPK is elevated. Pulmonary



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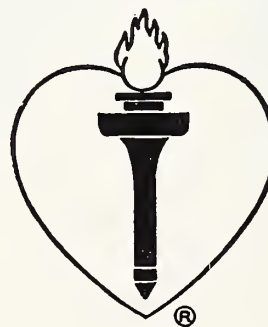
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function testing when available has demonstrated a restrictive defect.<sup>4</sup>

Treatment of PM-DM is yet somewhat uncertain. Prednisone in dosages of 40-60 mg./day for a month with tapering along with close monitoring of therapy by strength testing and serum CPK enzyme levels has been suggested.<sup>5</sup> Webb and Currie, 1972, re-emphasize, however, the importance of high dosage therapy in connective tissue disease and would submit that, as described by Vignos, Bowly and Watkins in 1964, a patient with PM-DM should not be considered steroid-resistant until he has failed to respond to 80-100 mg. of Prednisone daily.<sup>6</sup>

Corticosteroid therapy which leads to increased strength of the muscles of respiration and deglutition will ameliorate the forms of pulmonary involvement thought to be secondary to insufficient chest bellows action and recurrent aspiration; however, proof that interstitial inflammation and fibrosis will respond to steroids is unclear.<sup>2</sup>

Our patient two months after institution of corticosteroid therapy has shown good clinical, laboratory and radiologic response. She has tolerated Prednisone reductions to 30 mg. daily following an initial therapeutic dose of 60 mg./day.

Admission radiographs in this case report suggest a more acute inflammatory process and although histologic proof of such a reaction is lacking, it would seem that this patient's observed response to corticosteroid therapy would help to confirm that indeed her

parenchymal disease is of an acute nature. Schwartz, et al. have concluded from previous studies as well as their own 6 case review that the presence of active inflammation in lung biopsy is a predictor of good therapeutic response.<sup>4</sup>

Polymyositis-dermatomyositis in association with primary pulmonary disease is not common and primary pulmonary disease as the initial presentation of PM-DM is yet more infrequently reported. Webb and Currie, 1972, stress the importance of a careful search for occult muscle disease in patients with unexplained pulmonary fibrosis. In their review of the literature, two patients were reported with just such a presentation and polymyositis was not recognized before death.<sup>6</sup>

Muscle weakness may be attributed to general disability secondary to respiratory disease.<sup>6</sup> This is a masking effect of PM-DM that was present in our case. The relative acuteness of this patient's complaints heightened suspicions; however, previously reported cases have demonstrated instances of "masking" that have been much less obvious.

In further follow up of our patient with continued reduction of oral Prednisone the patient had increased muscle weakness and increased serum CPK, SGOT and LDH enzymes. However, chest x-rays remained free of recurrent pulmonary infiltrates and essentially stable with the last chest x-ray study done 10-20-78. Patient's symptoms and enzymes again responded to increasing oral Prednisone.

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# Minnesota Department of Health

## Nontuberculous Mycobacteria Isolated from Minnesota Residents During Period 1963-1975

HENRY BAUER, PH.D.,\* RICHARD FLYNN, B.A.,† KATHRINE L. GRAM‡

Distribution of 734 pathogenic nontuberculous mycobacteria (NTBM) isolated during period 1963-1975 from routine specimens obtained from 724 patients, residents of Minnesota, is presented. The highest infection rates (cumulative for 12-year period) per 100,000 persons were in the Northeastern and Northwestern health districts, 57.7 and 32.8 respectively. Of the ten recognized pathogenic NTBM, *M. simiae*, *M. szulgai* and *M. ulcerans* were not isolated during the 12-year period studied. The species name, Runyon's group, synonyms and common names of each are listed. Also a succinct statement of diseases caused, antituberculous drug susceptibility and distribution in nature is made for each of the 10 species.

OF THE MANY ACID-FAST bacilli that can be cultured and identified, ten mycobacteria species, other than *M. tuberculosis* and *M. bovis*, are currently recognized as causing disease in man.<sup>1</sup>

A bewildering number of terms and species names have been used to refer to these pathogenic mycobacteria. Effort to correct this confusion is being made.<sup>2</sup>

The purpose here is to identify the areas in Minnesota where pathogenic nontuberculous mycobacteria have been isolated from patients, and make brief comments about the ten mycobacteria and diseases they cause in man. The mycobacteria were isolated from routine specimens submitted by physicians whose patients resided in Minnesota.

The data was obtained from laboratory records in the Minnesota Department of Health.

### Nontuberculous Mycobacteria and Terminology

The term nontuberculous mycobacteria has been suggested when referring to groups of different acid-fast bacilli that are as distinct from each other as they are from *M. tuberculosis*.<sup>1,2</sup> Some of the confusion in terminology may be eliminated by using the species name and the term nontuberculous mycobacteria (NTBM) when referring to the group or when species name is not available. The diseases caused by these mycobacteria should be reported as

mycobacteriosis.<sup>2</sup>

The recognized clinically significant species of NTBM including Runyon's group designation, the synonyms and common names, disease caused in humans, drug susceptibility and distribution in nature are as follows:

#### *M. avium complex*

*M. avium*, *M. intracellulare*, *M. intracellulare-avium*, *M. battey*, avian tubercle bacilli, Battey bacilli, Battey-avium-swine complex, Battey-avium complex, Group III nonphotochromogen. There are at least 28 serotypes.<sup>1</sup> Most often cause pulmonary disease in humans, other forms of diseases are adenitis, skin lesions, kidney involvement, osteomyelitis and disseminated mycobacteriosis.<sup>3</sup> These bacteria exhibit multiple drug resistance, and as a rule chemotherapy is unsuccessful with the standard two or three drug regimen; 77% of patients receiving up to six drugs were treated successfully. Surgical excision is a reasonable alternative in a select group of patients.<sup>4,5</sup> These organisms have been isolated from soil, swine, birds, chickens, milk, cattle<sup>3</sup> and house dust.<sup>10</sup>

#### *M. chelonae*

*M. abscessus*, *M. chelonae* subspecies *abscessus*, *M. borstelense*, *M. runyonei*, *M. fortuitum-chelonae* complex, Group IV rapid grower. One serotype.<sup>1</sup> Has been isolated from puncture wounds<sup>6</sup> and occasionally from sputum with and without disease,<sup>7,8</sup> resistant to antituberculosis drugs.<sup>6,7</sup> Has been isolated from soil.<sup>8</sup>

#### *M. fortuitum*

*M. fortuitum-chelonae* complex, Group IV rapid

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grower. Two serotypes.<sup>1</sup> Has been isolated from infection abscesses, wounds, less frequently from lung abscess which appears to develop upon predisposing conditions such as achalasia, emphysema, previous tuberculosis and lipid pneumonitis.<sup>3,9</sup> Resistant to antituberculosis drugs.<sup>3,9</sup> Has been isolated from soil, water,<sup>8</sup> and house dust.<sup>10</sup>

*M. kansasii*

*M. luciflavus*, yellow bacillus, Group I photochromogen. One serotype.<sup>1</sup> Most often causes pulmonary disease, clinically and radiologically indistinguishable from tuberculosis.<sup>11</sup> Less common are urinary tract infections,<sup>13</sup> bone and joint disease.<sup>14</sup> Natural habitat unknown. Occasionally associated with lesions in lungs or lymph nodes of deer, swine and cattle, has also been isolated from water.<sup>8</sup> Initial chemotherapy with isoniazid, ethambutol and streptomycin with alternative programming containing rifampin has been suggested.<sup>12</sup>

*M. marinum*

*M. platyepiscus*, *M. balnei*, Group I photochromogen. Provisionally two serotypes.<sup>1</sup> Causes chronic granuloma of the skin in man.<sup>15</sup> The lesions are most often located on the arms or legs; often called "swimming pool granuloma". Open wound, abrasion or laceration of skin exposed to water contaminated with the organism appear to be a prerequisite to infection.<sup>16</sup> The disease may simulate lymphatic sporotrichosis. The organism is susceptible to rifampin and ethambutol<sup>17</sup> and most strains also susceptible to ethionine, D-cycloserine, pyrazinamide, viomycin and kanamycin.<sup>18</sup> Isolated from diseased fish, contaminated swimming pool, fish aquarium or tank.<sup>8,15</sup>

*M. simiae*

*M. habana*, Group I photochromogen. One, maybe two, serotypes. Has been isolated from bronchial washings and sputum from patients with pulmonary disease, in some instances in association with *M. tuberculosis*.<sup>1</sup> These organisms are highly resistant to antituberculosis drugs.<sup>5</sup> Recovered from monkeys imported from India and tap water in a hospital which had its own well.<sup>1</sup>

*M. scrofulaceum*

Group II Scotochromogen. Three or maybe four serotypes.<sup>1</sup> May cause lymph node disease especially in children,<sup>19</sup> may invade pre-existing pulmonary lesions, otherwise rarely causes disease. In vitro susceptibility of this organism to antituberculosis drugs varies widely, there is no predictable pattern.<sup>14</sup> Isolated from raw milk, other dairy products, pooled

oysters, soil and water.<sup>1</sup>

*M. szulgai*

Group II Scotochromogen. One serotype. Isolated from patients with chronic pulmonary disease simulating pulmonary tuberculosis, from tissue and aspirated fluid, from two patients with olecranon bursitis, one child with cervical lymphadenitis, and one case of extensive cutaneous infection in a patient with sarcoidosis on long term steroid medication.<sup>1,20</sup> Most strains are only slightly more resistant than *M. tuberculosis* to most of the antimycobacterial drugs. All isolates have been in association with human disease, except one isolate from tropical fish.<sup>21</sup>

*M. ulcerans*

*M. buruli*. Apparently one serotype.<sup>8</sup> Causes a chronic, indolent, extensively spreading ulceration of the skin. The necrotic process may involve the muscles. Lesions most often located on the exterior surface of the limbs but can locate in the abdomen, thorax and face. The disease has been seen in Australia, Malaya, New Guinea, Mexico and Africa,<sup>3,8</sup> not known to occur in the United States.<sup>14</sup> Reports indicate that most strains are susceptible to rifampin, streptomycin and cycloserine but resistant to isoniazid, ethambutol, PAS and ethionamide.<sup>1</sup> Available literature gives only humans as source of organism.

*M. xenopi*

*M. littorale*, Group III nonphotochromogen. Apparently one serotype.<sup>22</sup> Isolated from patients with pulmonary disease which is clinically and radiologically similar to tuberculosis. Has been found especially in England and Wales.<sup>23</sup> Also reported from patients in some mainland European countries, Australia and the United States. The organism is relatively drug susceptible, isoniazid, rifampin and streptomycin are recommended. Isolated from skin lesion of toad, hot and cold water taps, hot water generators and storage tanks of a hospital, bird droppings, various animals and their products.<sup>1</sup>

### Clinical Significance of Nontuberculous Mycobacteria

The nontuberculous mycobacteria have been isolated from many sources in nature, from animal tissue, milk, other dairy products, house dust and from sputum, saliva and gastric washings of clinically well persons.<sup>3,8,10,15,16</sup> Accordingly the etiologic significance of such mycobacteria must be carefully evaluated, especially if the organism is isolated from superficial lesions and pulmonary secretions.



TABLE 1  
Pathogenic Nontuberculous Isolates (1963-1975) from 724 Minnesota Resident Patients  
According to Specimens and, Where Available, Physician's Diagnosis

	Total				Sputum			Gastric			Bronchial Washings			Urine			Tissue			Other		
	Diagnosis																					
	Persons	Isolates	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data	Total	Accepted	Insuffi- cient data
M. avium complex	474	474	57	417	349	39	310	49	2	47	16	2	14	21	1	20	22	10	12	17	3	14
M. chelonai	3	3	1	2	2		2													1	1	
M. fortuitum	97	97	12	85	79	8	71	9		9	2		2	2		2	4	3	1	1	1	
M. kansasii	54	54	37	17	38	22	16	5	5		2	2		1		1	6	6		2	2	
M. marinum	5	5	5														5	5				
M. scrofulaceum	78	78	15	63	34	4	30	13	2	11	3		3	5		5	15	9	6	8		8
M. xenopi	3	3		3	2		2				1		1									
M. avium complex and M. scrofulaceum	5	10	2	3	5	2	3															
M. avium complex and M. chelonai	2	4	1	*1	1	1											1		*1			
M. avium complex and M. fortuitum	3	6		3	3		3															
Total	724	734	130	594	513	76	437	76	9	67	24	4	20	29	1	28	53	33	20	29	7	22

\*M. avium isolated from sputum, and M. cheionei from arm tissue of same patient.

TABLE 2  
Distribution of Pathogenic Nontuberculous Mycobacteria Isolated,  
Minnesota Resident Patients, 1963-1975 Inclusive

Health District and Population	No. of Persons	*Rate per 100,000	M. avium complex		M. chelonai		M. fortuitum		M. kansasii		M. marinum		M. scrofulaceum		M. xenopi		Total
			No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	
Northeastern (346,424)	200	57.7	168	48.5			13	3.8	8	2.3	1	.3	14	4.0			204
Northwestern (149,173)	49	32.8	35	23.5			7	4.7	1	.7			6	4.0			49
West Central (182,251)	23	12.6	10	5.5			5	2.7	3	1.6			5	2.7			23
Central (357,779)	52	14.5	33	9.2	1	.3	7	2.0	3	.8			9	2.5			53
Metropolitan (1,874,612)	277	14.8	156	8.3	2	.1	49	2.6	34	1.8	3	.2	34	1.8	3	.2	281
Southwestern (293,241)	38	12.9	27	9.2	1	.3	5	1.7	2	.7			3	1.0			38
South Central (218,077)	28	12.8	15	6.9	1	.5	9	4.1			1	.5	3	1.4			29
Southeastern (384,546)	57	14.8	40	10.4			5	1.3	3	.8			9	2.3			57
State Total (3,806,103)	724	19.0	484	12.7	5	.1	100	2.6	54	1.4	5	.1	83	2.2	3	.08	734

\*12-year accumulated infection rate based on 1970 census. M. szulgai, M. simiae, and M. ulcerans not isolated in Minnesota.  
Northeastern District Counties: Aitkin, Carlton, Cook, Itasca, Koochiching, Lake, Pine, St. Louis.  
Northwestern District: Beltrami, Clearwater, Hubbard, Kittson, Lake of Woods, Mahanomen, Marshall, Norman, Pennington, Polk, Red Lake, Roseau.  
West Central District: Becker, Big Stone, Clay, Douglas, Grant, Otter Tail, Stevens, Traverse, Wilkin.  
Central District: Benton, Cass, Chisago, Crow Wing, Isanti, Kanabec, Mille Lacs, Morrison, Pope, Sherburne, Stearns, Todd, Wadena, Wright.  
Metropolitan District: Anoka, Carver, Dakota, Hennepin, Ramsey, Scott, Washington.  
Southwestern District: Chippewa, Cottonwood, Jackson, Kandiyohi, Lac qui Parle, Lincoln, Lyon, McLeod, Meeker, Murray, Nobles, Pipestone, Redwood, Renville, Rock, Swift, Yellow Medicine.  
South Central District: Blue Earth, Brown, Faribault, LeSueur, Martin, Nicolet, Sibley, Waseca, Watonwan.  
Southeastern District: Dodge, Fillmore, Freeborn, Goodhue, Houston, Mower, Olmsted, Rice, Steele, Wabasha, Winona



Isolation of mycobacteria, other than tubercle bacilli, may have significance if one or more of the following situations is demonstrable: (1) evidence such as an infiltrate visible on a chest roentgenogram, of disease, the cause of which has not been determined by careful clinical and laboratory studies, (2) isolation of the same strain of mycobacteria repeatedly usually in absence of other pathogens, (3) isolation of mycobacteria from a closed lesion from which the specimen has been collected and handled under sterile condition, for example an abscess or biopsy tissue.<sup>24</sup>

Occasionally, more than one species of NTBM may be isolated from the same patient and specimen source,<sup>5</sup> Table 1. Thus interpretation of the guidelines must be made in relation to the kind and frequency of the mycobacterium isolated from repeated specimens as well as the extent and nature of the lesion. For example, *M. avium* complex and *M. scrofulaceum* were isolated from sputum of five patients. In one patient, a miner, *M. scrofulaceum* was accepted as causal agent of the pulmonary disease. In another patient, a welder, with silicosis, "unclassified *Scotochromogens*" (presumably *M. scrofulaceum*) were isolated from four of five consecutive sputum specimens and *M. scrofulaceum* was isolated from one specimen. *M. avium* complex was isolated from two sputum specimens collected between one to two years later. The physician made the diagnosis of mycobacteriosis after the repeated isolation of "unclassified *Scotochromogens*".

Sputum, 513, and gastric washings, 76, were the predominant specimens received in the laboratory, Table 1. The *M. avium* complex was isolated most often from these two and other specimens. Of the 474 persons from whom *M. avium* complex was isolated, the attending physician accepted the organism as the causal agent of disease for 57 (12%) patients. Because of insufficient data we do not know the diagnosis for the remaining 417 patients.

The presence of *M. kansasii* was accepted as the cause of disease in 37 (69%) of 54 patients, the data for 17 patients was insufficient to determine their status. Thirty-five of the 37 diagnosed patients had pulmonary infections, one had infection of the left inguinal area and testes, and one had infection of the ulnar bursa. This high percentage of acceptance was not observed for any other organism except *M. marinum* (100%).

It appears that physicians more readily accepted isolates from tissue as the infecting agent than from any other specimens. Of 53 from whom tissue specimens were submitted for culture, 33 (62%) were diagnosed as being infected with the NTBM isolated.

The absence of the physician's diagnosis hampered the interpretation of the data in Table 1.

### Epidemiology

The epidemiology of diseases attributable to the NTBM has not been well delineated. The distribution of these organisms in nature and the occurrence of most species in apparently well persons appear to complicate current limited epidemiology. There is no clear evidence of person-to-person transmission of NTBM species.<sup>1</sup> Host tissue damage in some instances predisposes to infection.<sup>1,11,14,16</sup>

Skin sensitivity testing with PPD-B (Battey) suggests some persons apparently become infected without overt disease. In 1973-4 we did skin sensitivity tests with PPD-B (obtained from Center of Disease Control) and PPD-tuberculin (commercial product equivalent to the standard PPD-s) on 3,228 school children and personnel in St. Louis, Cook and Carlton counties. We found 38 (1.2%) showed a reaction of 10 mm or greater with PPD-B, of which one adult was positive at 10 mm to both. None of the children showed reaction of 10 mm with PPD-tuberculin.<sup>27</sup> Cross reactions to some of the NTBM induced by tuberculous infection do occur and vice versa.<sup>26</sup> These reactions are generally smaller than specific reactions induced by the specific PPD; however, there is considerable overlap in size. Thus the larger the size of a particular reaction the more likely it is to be specific.<sup>1,25,26</sup> Edwards et al.<sup>25</sup> did skin sensitivity tests from 1958-1965, on 9,020 white male navy recruits, ages 17-21 (lifetime Minnesota residents) with PPD-S (tuberculin prepared by Seibert), PPD-B and Histoplasmin. Of the 9,020 tested with PPD-B, 1,773 (19.7%) showed reaction of 4 mm or greater. They chose the 4 mm or more of induration to separate those who reacted to the test from those who did not. They stated that among the navy recruits who had very low rates of tuberculosis infection the PPD-B may be regarded as a measure of NTBM infections. When tested with PPD-S, 165 (1.8%), showed reaction of 10 mm or greater. Applying the 10 mm and greater criteria to the PPD-B group, there were 499 (5.5%) reactors.

The health districts, residence of 724 patients from whom 734 NTBM were isolated are shown in Table 2. The highest isolation rate per 100,000 residents, was 57.7 and 32.8 for the Northeastern and Northwestern districts respectively. Either one or the other of these districts also showed the highest rate of NTBM isolates for all species except *M. chelonae*, *M. marinum* and *M. xenopi*. The highest isolation rate per 100,000 for the state was 12.7 for *M. avium* complex, and when



compared with the districts the isolation rate for this organism was highest in Northeastern and Northwestern districts, 48.5 and 23.5 respectively.

Of the ten recognized pathogenic NTBM, *M. simiae*, *M. szulgai* and *M. ulcerans* were not isolated from Minnesota residents during the period 1963-1975. Infection with *M. ulcerans* is not known to occur in the United States.<sup>14</sup>

### Comments

Laboratory procedures for the identification of mycobacteria are so widely published it is no longer defensible to designate the nontuberculous mycobacteria as "atypical", "unclassified" or by Runyon's classification.

Serotyping of the NTBM should be instituted, especially for isolates such as *M. avium* complex and *M. scrofulaceum*. Such data is needed for epidemiology and specific characterization of clinically significant NTBM.

It is suggested, when tuberculosis is suspected, the term mycobacteriosis be used to designate the patient's disease until there is laboratory and clinical evidence to support the term tuberculosis. In our study of 32 patients with X-ray evidence of pulmonary infection, the diagnosis for 16 (50%) was "suspected tuberculosis". The diagnosis was changed to *M. kansasii*

infection or mycobacteriosis after *M. kansasii* was isolated.<sup>27</sup> Accordingly it is necessary that *M. tuberculosis* and *M. bovis* be distinguished from other mycobacteria for the following reasons: (1) tuberculosis is a contagious disease whereas according to current concept, infection with other mycobacteria is not; (2) patients with tuberculosis may be subject to certain health regulations, such as compulsory hospitalization which do not apply to other mycobacterial diseases; (3) specific antimicrobial therapy may be different for patients with tuberculosis as compared to other mycobacterial infections; (4) epidemiologic data are of no value unless the mycobacterium causing a suspected infection is identified; (5) morbidity records will be inaccurate.<sup>14,27</sup>

Our knowledge of NTBM and their association with disease in man has been achieved through the cooperation of practicing physicians, bacteriologists and public health personnel. Continued cooperation, more definitive laboratory identification of the NTBM, more intensive epidemiology and detailed records are necessary to better understand the individual case and public health implications.

The state department of health should be the state control center, gathering, collating, evaluating and publishing data about the nontuberculous mycobacteria in the environment and associated with disease.

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# Special Article

## Simple Method to Measure the Distensibility of the Pulmonary Vascular System in the Intact Animal

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The relationship between the volume of blood and the hydro-static pressure within the pulmonary vascular system was studied.

Acute hypervolemia was produced in ten anesthetized dogs. The volume of blood within the lungs and the left side of the heart (LLHV) was determined by the indicator dilution technic. Pulmonary artery and pulmonary artery wedge pressures were recorded simultaneously.

During the production of hypervolemia there was a positive, approximately linear correlation between the LLHV and the pulmonary artery mean pressure (PAm). Statistical analysis allowed calculation of an average line for all of the experiments. The slope of this line using a 95 percent confidence interval was  $7.3 \pm 1.0$  ml/mm Hg.

Distensibility is defined as the ratio of a change in volume for a change in pressure. Since during the production of hypervolemia the pressure increased equally throughout the pulmonary vascular system, the slope of the curve relating LLHV to PAm represented the distensibility of the lungs and the left side of the heart.

Thus, the production of acute hypervolemia is a simple method for studying in the intact animal the distensibility of the pulmonary vascular system taken as a whole.

THE DISTENSIBILITY of the pulmonary vascular system can be defined as the ratio of a change in intravascular volume to a change in intravascular transmural pressure. Distensibility is an important characteristic since it determines the ability of the pulmonary vascular system to accept an increase in volume. It is also a consideration in the pressure levels reached and the pulse contour produced within the circuit.

A variety of technics and approaches have been used to study pulmonary vascular volume and pressure both in animals and in man<sup>1</sup>. Information about the relationship between these two variables (i.e., the distensibility) has been obtained from experiments using animal preparations<sup>2</sup>, isolated lungs<sup>3</sup>, and lung lobes<sup>4</sup>. It is difficult, however, to assemble from studies of the separate parts a comprehensive picture of the distensibility of the pulmonary vascular system

taken as a whole.

In the present study acute hypervolemia was produced in a group of ten dogs, and interesting simultaneous changes in pulmonary intravascular volume and pressure were observed. The data suggested a simple method which can be used to determine the distensibility of the pulmonary vascular system in the intact animal.

### Methods

Ten mongrel dogs weighing from 7.3 to 9.6 Kg were studied. Surgical anesthesia was induced by the intravenous injection of morphine sulfate, 5 mg/Kg, and chloralose 55 mg/Kg. This anesthetic was chosen in order to achieve a relatively slow heart rate. Additional anesthetic was given during the course of the experiment as needed.

The dogs were placed on an operating table and needle electrocardiographic leads attached. Respirations were recorded using a nose attachment containing a thermocouple which detected the difference in temperature between the inspired and expired air.

The neck was shaved and the right jugular vein and the carotid arteries exposed. Three Cournand No 6 cardiac catheters 125 cm in length were passed through

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the jugular vein. Catheter position was monitored by displaying the pressure pulse on a Rycom Model RM 24 oscilloscope. One catheter was placed in the pulmonary artery for recording pulmonary artery pressure. One catheter was positioned in the pulmonary artery "wedge" position in order to obtain a measurement of the pulmonary venous or left atrial pressure<sup>5,6</sup>. The third catheter was placed with its tip just above the pulmonic valve and was used for injecting indicator dye.

A polyethylene number 260 catheter 50 cm in length was inserted through the right carotid artery and in seven dogs the left ventricle was entered in the retrograde direction. The catheter tip was positioned just above the aortic valve by monitoring pressure as the catheter was slowly withdrawn from the left ventricle into the aorta. The aortic valve could not be crossed in three dogs. The supra-aortic catheter was used for sampling blood during the dye dilution studies.

A second polyethylene number 260 catheter was passed through the left carotid artery into the aortic arch and used to record central aortic pressures. A third such catheter was used for rapid infusion of fluid; in eight dogs this catheter was passed through the femoral artery into the aorta, and in two dogs was placed in the femoral vein.

The zero pressure reference level was taken as one-half the antero-posterior chest diameter. Pressures were recorded using Statham p23Db strain gauges. Mean pressures were obtained either by hydraulic damping or by planimetric integration of the recorded pressure pulse.

Quantitative indicator dilution studies were done using indocyanine green dye and a Waters X-250 densitometer. For valid volume calculations from indicator dilution curves the indicator must be well mixed over a cross-sectional area between the injection and sampling sites. This requirement was satisfactorily met by injecting just distal to the pulmonic valve and sampling just distal to the aortic valve<sup>7</sup>.

The densitometer was previously shown to respond linearly to increasing dye concentrations up to 45 mg/l. Two ml of dye containing 1.25 mg/ml were injected from a calibrated syringe into the pulmonary artery injection catheter which had previously been over filled with the dye. Blood was sampled using a Gilford withdrawal-infusion pump at 31.6 ml/min. The total volume of the sampling catheter, connectors, and one-half the volume of the densitometer was 1.5 ml. Dye calibration curves were carried out for each dog, and all dye calibrations were carried out in

duplicate.

The fluids used for infusion included plasma, whole blood, normal saline, and 10 percent Rheomacrodex in normal saline (dextran). Dextran was given to six dogs, saline to one, and whole blood to one. One dog received plasma followed by dextran, and another received saline followed by dextran. The fluid was injected manually at a rate of two to three ml/sec in increments of 150 or 200 ml. Thirty ml of blood were withdrawn for further dye curve calibrations after each infusion.

A Honeywell Visicorder 1508 multichannel recorder was used. The following were recorded simultaneously: a standard lead of the electrocardiogram; respirations; dye dilution curves; and pulmonary artery, pulmonary artery wedge, and central aortic pressures. Two consecutive determinations were recorded within three to five minutes.

The injection time was corrected for the lag caused by the catheter withdrawal system. Cardiac outputs and mean transit times were determined from the dye dilution curves by the method of Stewart-Hamilton<sup>8,9</sup>. The volume of blood between the tip of the injection catheter which was just distal to the pulmonic valve, and the sampling catheter which was just distal to the aortic valve were calculated as the product of the cardiac output and the mean transit time. This volume thus includes that of the lung vessels and the left side of the heart (LLHV).

In these studies of the pulmonary circulation it would have been advantageous to have been able to exclude the left heart volume and to measure the pulmonary blood volume alone. An approach to this is to calculate the volumes from dye dilution curves obtained by injecting dye successively into both the pulmonary artery and the left atrium with sampling from a systemic artery. The difference between these two volumes, however, would presumably represent not only the volume of the lungs alone, but also, an unknown contribution by the left atrium.

Corcondilas and Shepherd<sup>10</sup> calculated the lung volume and the LLHV in dogs. They found that the reproducibility was much better for the LLHV measurements. In their experiments the LLHV was 12 ml/Kg, with a range of 8 to 17 ml. This is similar to the figure obtained in the present study.

## Results

The average value for the lungs and left heart volume (LLHV) in the ten dogs during the control period was 15.6 ml/Kg body weight, with a range of 10.5 to 21.6 ml/Kg. The average difference for



consecutive determinations was five percent, and the greatest difference was nine percent.

As the LLHV increased following the production of hypervolemia the pulmonary artery mean pressure (PAm) also increased. The maximum change in the pulmonary artery mean pressure was at least twofold in nine of the ten dogs.

In Figure 1 LLHV was plotted against the simultaneously measured PAm. The first experiment was eliminated because too few measurements were available to insure reliability of the slope of their plot. The statistically calculated average line<sup>11</sup> had a slope within a 95 percent confidence interval of  $7.3 \pm 1.0$  ml/mm Hg. This line is shown in Figure 1. The scatter of the points was not appreciably reduced when the LLHV divided by body weight was plotted against PAm. This was to be expected since the dogs were of similar weight.

It is generally agreed that the pulmonary artery wedge pressure can be used as an adequate measurement of the pulmonary venous or left atrial pressure<sup>5,6</sup>. The present data indicated that with the production of hypervolemia there was a rise in mean pressure throughout the pulmonary vascular system. In five of

the seven experiments in which sufficient measurements were available the increase in PAm equalled the increase in the pulmonary artery wedge mean pressure. One dog was unusual in that during the experiment the respirations were labored, the pulmonary artery wedge mean pressure was initially negative, and the stomach and intestines became greatly distended with air.

### Discussion

The heart may be considered to consist of two pumps connected in series. Since the contractions of the two ventricles are approximately synchronous, blood which was ejected from the right ventricle in systole must be temporarily stored somewhere between the pulmonic and mitral valves until the ensuing diastole when it can then enter the left ventricle. For the purpose of this discussion the storage sites may be divided into four segments, namely, pulmonary artery, pulmonary capillaries, pulmonary veins, and left atrium.

The distensibility,  $D$ , of a vascular segment is equal to the ratio of a change in volume,  $V$ , for a change in pressure,  $P$ , or,  $D = \Delta V / \Delta P$ . Therefore, we can write an equation for the distensibility of each of the segments as follows:

$$D_{pa} = \Delta V_{pa} / \Delta P_{pa}$$

$$D_{pc} = \Delta V_{pc} / \Delta P_{pc}$$

$$D_{pv} = \Delta V_{pv} / \Delta P_{pv}$$

$$D_{la} = \Delta V_{la} / \Delta P_{la}$$

where  $pa$  = pulmonary artery,  $pc$  = pulmonary capillaries,  $pv$  = pulmonary veins, and  $la$  = left atrium.

It should be noted that each  $\Delta P$  refers to the change in transmural pressure associated with a change in volume within the segment and does not refer to the pressure gradient along the segment.

By definition, if we were able to measure the volume change for a given pressure change in each of these segments we could calculate the distensibility of each segment. If the equation for each segment had the same denominator it is obvious that the total distensibility of the segments taken together,  $D_{pa,la}$ , could be expressed as the sum of the individual distensibilities, or,  $D_{pa,la} = D_{pa} + D_{pc} + D_{pv} + D_{la}$ . Therefore, in order to calculate  $D_{pa,la}$  one would not need to determine the change in volume in each segment provided that a known change in pressure occurred equally in each

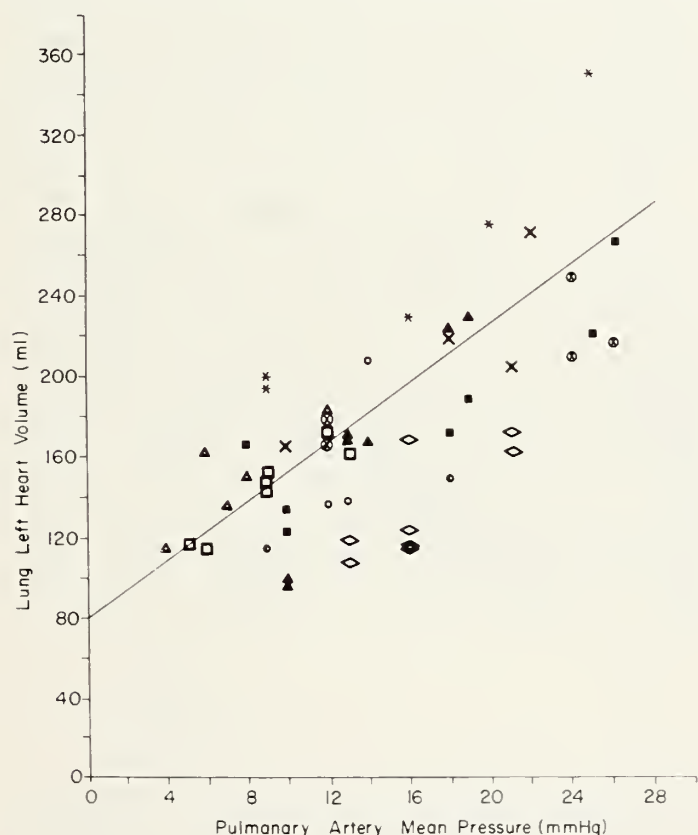


Fig. 1 — The volume of blood in the lungs and left side of the heart in ml for the individual experiments is plotted against the simultaneously measured pulmonary artery mean pressure in mm Hg. The straight line is the calculated average line<sup>11</sup>. This line has a slope, within a confidence interval of 95 percent, of  $7.3 \pm 1.0$  ml/mm Hg.



segment and that the sum of the individual volume changes could be measured. In this study the lung left heart volume (LLHV) was used to estimate the total volume contained within the system. Under these conditions, then, the equation for the distensibility of the pulmonary vascular system may be written as  $D_{pa,la} = \Delta LLHV / \Delta P_{pa,la}$ , where  $\Delta P_{pa,la}$  is the pressure change which occurred equally throughout the system.

Figure 1 shows that in the acute hypervolemia experiments there was a good positive correlation between the change in LLHV and the change in pulmonary artery mean pressure (PAm). Statistical analysis<sup>11</sup> showed that the average slope of the plot of LLHV against PAm, within a 95 percent confidence interval, was  $7.3 \pm 1.0$  ml/mm Hg.

The close positive correlation between LLHV and PAm was in agreement with the studies of perfused isolated dog lungs reported by Sarnoff and Berglund.<sup>3</sup> The slope of the volume pressure curves in their experiments equaled 7 ml/mm Hg. Similar results were found by Sarnoff, Berglund and Sarnoff<sup>4</sup> when they estimated changes in pulmonary intravascular volume by measuring changes in the weight of lung lobes in the intact dog.

Lindsey and Guyton<sup>2</sup> used radioactive serum albumin in dogs to determine changes in blood volume. The pulmonary artery pressure was also measured. They found that the volume pressure curve in their experiments was comparable to that of Sarnoff and Berglund and concluded that the same volume pressure relationship operated in the intact as in the isolated lung. A similar relationship between pulmonary intravascular volume and pressure has also been observed in man<sup>12,13</sup>.

Feeley, Lee and Milnor<sup>14</sup> studied changes in LLHV and PAm in dogs following injection of epinephrine, norepinephrine, isoproterenol, and histamine. Figure 2 is the same as Figure 1 with the addition of data taken from the experiments of Feeley et al. The plot of the results from their pharmacologic experiments fitted well with those from the present hypervolemia study.

Although the data in the hypervolemia study were reproducible and were consistent with those reported in the literature, further evidence is necessary before the slope of the plot of LLHV against PAm can be accepted as representing the distensibility of the pulmonary vascular system. This is because, as mentioned above, the denominator in the equation  $D_{pa,la} = \Delta LLHV / \Delta P_{pa,la}$  requires that the same change in pressure occur in each of the segments comprising the pulmonary vascular system. In the present experiments the

production of acute hypervolemia in intact anesthetized dogs usually was associated with an equal rise in mean pressure in both the pulmonary artery and the pulmonary artery wedge positions.

The occurrence of an equal increase in pressure throughout the pulmonary vascular tree and the left side of the heart has been observed by others in experiments on intact animals. Gauer, Henry and Sieker<sup>15</sup> reported an equal rise in left atrial and pulmonary artery mean pressures after transfusion. Fowler, Franch and Bloom<sup>16</sup> found that the PAm increased following expansion of the plasma volume in two dogs and was associated with a similar elevation of the left ventricular diastolic pressure. Feeley, Lee and Milnor<sup>14</sup> infused epinephrine and norepinephrine into dogs and found an increase in LLHV. In two dogs simultaneous measurements showed an identical rise in pressure in the left ventricle and the left atrium.

The simultaneous and equal rise in pressures in the pulmonary vasculature and the left atrium has also been reported in experiments using lung preparations. Sarnoff and Berglund<sup>3</sup> perfused dog lungs by a motor driven pump. They found that the injection of a volume increment into the pulmonary artery produced similar

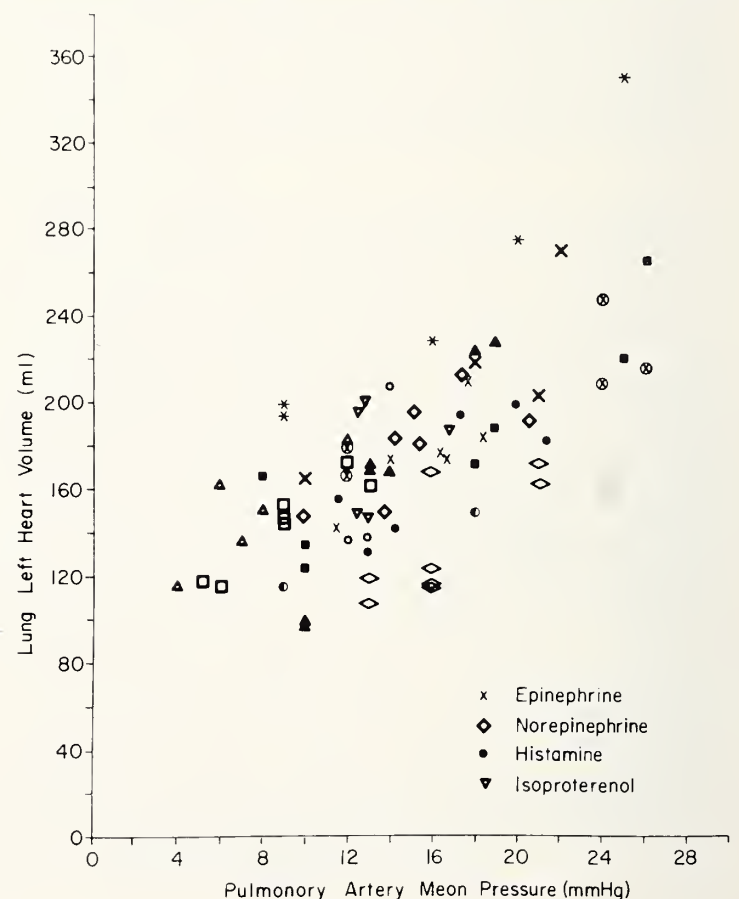


Fig. 2 — Figure 2 is a replot of Figure 1 with the addition of points taken from the data of Feeley, Lee, and Milnor<sup>14</sup>. These authors studied both closed and open-chested dogs in the control state and with the administration of epinephrine, norepinephrine isoproterenol and histamine.



pressure changes in the pulmonary artery and the left atrium.

In two of the seven present experiments a parallel rise in the mean pulmonary artery and pulmonary wedge pressures did not occur with the production of hypervolemia. There are several possible explanations. The recorded pulmonary artery wedge pressures would have been erroneous if the catheter tip had not been properly wedged into a small pulmonary artery branch. The pressures would also have been incorrect if the luminal continuity anywhere from the catheter tip to the pulmonary vein draining that segment were interrupted, as, for example, by a blood clot. In addition, the acute increase in pulmonary blood volume and pulmonary capillary pressure produced by the hypervolemia could have resulted in interstitial and alveolar edema.

It should be noted that the data presented in this paper refer only to the state which existed in the animal immediately after injection of the volume increment. No statement may be made about any alterations or adjustments which may have occurred in the animal at a later time.

As seen in Figure 2, both the results of the acute hypervolemia experiments and the data taken from the pharmacologic experiments of Feeley et al.<sup>14</sup> showed the same approximately linear relationship between LLHV and PAm over the entire range studied. Finding the same results from these two different methods of investigation suggests that the increase in LLHV was accounted for by vascular segments increasing their volume according to their distensibility rather than by the opening of new channels. For the latter mechanism to be importantly operative the opening pressure of the channels would have to be distributed throughout the entire pressure range studied. Additional channels must progressively become available as the PAm increases and reaches their opening pressures, and this new volume would have to be added to the LLHV in the same proportion to the increase in PAm.

Otherwise, the slope of the plot of LLHV against PAm would not remain approximately linear. This implies that the recruitment of previously closed channels probably was not a major factor in determining the observed relationship between LLHV and PAm.

There is also evidence in the literature that the contribution to an increase in LLHV by the opening of previously closed pulmonary capillaries is likely to be limited. Daly, Giammona and Ross<sup>17</sup> studied the effect of body tilting and G suit inflation on the pulmonary capillary volume. They found that the pulmonary capillary volume would increase or decrease over a small pressure range but then plateaued and changed no more even with large changes in pressure. Consequently, it appears that the opening of pulmonary capillaries could play a role in the accommodation of an increase in LLHV associated with small pressure changes but would not adequately explain the continued linear relationship between LLHV and PAm at greater pressure ranges. This view is consistent with the work of Karatzas and Lee<sup>18</sup> who showed that up to about 70 percent of the right ventricular stroke volume is stored in the precapillary vascular segments.

The linear relationship of LLHV and PAm in the present experiments, therefore, can be mainly attributed to the uptake of the increased volume within the pulmonary vascular system according to its distensibility. Since the production of acute hypervolemia was accompanied by an equal rise in pulmonary artery and pulmonary artery wedge mean pressures, the equation  $D_{pa,la} = \Delta LLHV / \Delta P_{pa,la}$  may be used. This offers a simple way to measure in the intact animal the distensibility of the pulmonary vascular system taken as a whole. Thus, the average slope of the plot of LLHV against PAm of  $7.3 \pm 1.0$  ml/mm Hg can be taken to represent the distensibility of the pulmonary vascular system in the living dog.

#### Acknowledgments

We are grateful to Mr. Richard Pogue and Dr. Robert Evans for the statistical analysis, and to Dr. Maurice Visscher for his advice.

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- 12.-18. Will be found on page 242.



# Minnesota Medical Association

## MMA Annual Meeting — May 21-22, 1980

The 1980 Scientific Assembly will consist of courses on a wide variety of topics. Participants will have the opportunity to attend two half-day sessions or one all-day session on Wednesday, May 21, and again on Thursday, May 22. A preliminary schedule is listed below. Complete information on the Annual Meeting and registration material will be mailed in early April.

### WEDNESDAY, MAY 21, 1980

#### 8:30-11:30 A.M.

Diabetes Mellitus — New Approaches to an Old Disease

P. J. Palumbo, M.D., Course Director

Clinical Toxicology — A Brief Symposium

Kusum Saxena, M.D., Course Director

Safe and Effective Management of Office X-ray — The Physician's Role

Larry Stetzner, M.D., Ph.D., Course Director

Adolescent Medicine

Robert Blum, M.D., Course Director

#### 2:00-5:00 p.m.

Acid-Base and Electrolyte Disorders

Morris Davidman, M.D., Course Director

Practice versus Malpractice

Robert Brittain, M.D., Course Director

Occupational Medicine for the Practicing Physician

Paul Johnson, M.D., Course Director

Minnesota Health Care Directions: Alternatives for 1980

Eugene C. Ott, M.D., Course Director

#### All Day (9:00 a.m.-4:00 p.m.)

Neonatal Resuscitation

Mark Bixby, Course Director

### THURSDAY, May 22, 1980

#### 8:30-11:30 a.m.

Techniques of Preventive Medicine

Ellen Alkon, M.D., Course Director

Caring for Southeast Asian Immigrants

Robert Breitenbucher, M.D., Course Director

Crib Death (Sudden Infant Death Syndrome) — A Medical and Psychological Crisis

Joseph Leek, M.D., Course Director

#### 2:00-5:00 p.m.

Pediatric Problems

William Krivit, M.D., Ph.D., Course Director

Update in Clinical Virology

Henry Balfour, Jr., M.D., Course Director

Evaluation of the High-Risk Obstetrical Patient

Lyndon Hill, M.D., Course Director

#### All Day (8:30 a.m.-5:00 p.m.)

Annual Meeting of the Minnesota Chapter of the American College of Surgeons

Melvin Bubrick, M.D., and Claude Hitchcock, M.D., Course Directors



## AMA Delegates and Alternate Delegates Nominations

Delegates whose terms expire as of December 31, 1980 are Dr. Robert Kelly and Dr. Lloyd Bartholomew. However, inasmuch as Dr. Kelly has served six full terms of two years as an AMA Delegate, he is ineligible to be a candidate for re-election. The following candidates for AMA Delegates have been nominated by the Board of Trustees and will be voted upon at the House of Delegates Meeting in May at the Radisson South Hotel.

Lloyd Bartholomew, M.D. — Delegate  
William Jacott, M.D. — Delegate

The following two physicians have been nominated as Alternate Delegates.

James Halvorson, M.D. — Alternate Delegate  
Richard Tompkins, M.D. — Alternate Delegate

Dr. William Jacott's election as delegate would result in a vacancy of the office of alternate delegate. Provisional nomination is Dr. Ben Owens as AMA Alternate Delegate to replace Dr. Jacott in the event of Dr. Jacott being elected as Delegate. Dr. Halvorson is standing for re-election. Dr. G. Roy Diessner, whose term as alternate delegate expires, has chosen not to be a candidate for re-election.

Any delegate may make additional nominations from the House of Delegates floor after the report of the Nominating Committee.

Dr. George Martin of Thief River Falls serves as chairperson of the MMA Delegation to the AMA.

## 1980 MMA Leadership Conference

The Minnesota Medical Association will sponsor a Leadership Conference on Friday, June 27, 1980, at the Radisson South Hotel in Bloomington for members of the MMA Board, county medical society officers and staff, MMA committee chairmen and alternates, specialty society officers and representatives, and MMA Auxiliary leadership.

The 1980 MMA Leadership Conference is designed to bring together the leadership of organized medicine in Minnesota. Important goals of the conference are to enhance leadership skills, provide information on important issues, and to improve communications between all levels of leadership.

An all-day program is being planned. Professor Ernest Bormann of the University of Minnesota, a nationally recognized authority on meetings, will conduct a workshop on organizing and presiding over effective meetings. Following Professor Bormann, a Capitol Report session is planned consisting of a panel of government leaders reporting on developments effecting medicine.

Robert B. Hunter, M.D., AMA President-Elect, has been invited to speak at the noon luncheon. Afternoon presentations include MMA structure, membership, AMA delegation, MMA Auxiliary, and MINNPAC. Breakout sessions for county society officers, committee chairmen, and specialty society officers will conclude the day's activities.



## Classified Advertisements

Classified advertising rates are forty (40) cents a word; minimum monthly charge \$10.00, key number, \$1.50 additional. Replies to advertisements with key numbers should be mailed in care of Minnesota Medicine, 101 East 5th, Suite 900, St. Paul, Minn. 55101.

OPHTHALMOLOGIST WANTED IN SOUTHERN MINNESOTA Group Practice. The Albert Lea Clinic, P.A., in Albert Lea, Minnesota, a 16 man multi-specialty group is seeking a replacement for a senior man. Board certified or Board eligible. Salary guaranteed first year. Second year, participant in clinic's incentive income distribution plan. Low cost buy-in arrangement. Profit sharing plan. Top insurance plan with full range of other benefits. New hospital in city. A choice practice and exceptional place to live. Contact William Brouwer, Assistant Administrator, Albert Lea Clinic, P.A., 1602 Fountain Street, Albert Lea, Minnesota 56007, phone 507-373-8251, personal phone 507-889-6381 or contact Gary A. Boeke, M.D., 507-373-8251, personal phone 507-826-3288.

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FAMILY PHYSICIAN to join a group of seven. The clinic is in a rural community 40 miles north of the Mpls-St. Paul area. Modern clinic, excellent school system, churches woods and lakes nearby. Two ski areas are within 15 min; XC out your back door or 15 to 30 minutes of maintained trails. Fifteen miles to Scenic Wild River Area. One of the fastest growing counties in Minnesota. Full range of family practice with superb specialty coverage when you desire. Forty-nine bed modern hospital (9 yrs), new clinic (1974) and 268 nursing beds in the community. Salary first year, maximum fringe benefits, no buy in, very liberal education and vacation time. Contact: Chris P. Ceman, M.D., Chisago Lakes Medical Center, P.A., Chisago City, MN 55013, (612) 257-1190.

OBSTETRICIAN/GYNECOLOGISTS — FAMILY PRACTITIONERS — Multispecialty Group of 28 physicians is offering practice opportunity to: — Obstetrician/Gynecologists — to join 4 member department — Family Practitioners — to join 8 member department. Attractive income offering and excellent fringe benefits; modern, well-equipped Clinic Building and Hospital; medical school teaching appointment available. A.A.A.H.C. accredited facility and C.A.P. accredited laboratory. Satellite practice location also available. Excellent educational system and facilities. Recreational activities — exceptional locally, and your choice outside of area within three hours traveling. Contract J. E. Hartfield, M.D., Medical Director, or F. J. Wilkus, FACMGMA, Administrator, Olmsted Medical and Surgical Group, P.A., 210 Ninth Street, S.E. Rochester, Minnesota 55901, or call (507) 288-3443.

ANESTHESIOLOGIST needed in outstate Minnesota. Should be board certified or eligible. Department has 300+ cases per month. Malpractice insurance paid. \$60,000 first year, then buy in. Write: Minnesota Medicine — 547, Suite 900, 101 E. 5th St., St. Paul 55101.

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# President's Letter

Over the past eleven months, I have made a sincere effort to make the President's Letter carry a message of some kind. I have no idea how often those messages were communicated or how they were received. I hope that some of you have, occasionally, found food for thought in the letter. Today I have no specific message but rather only random thoughts.

It has long been my thought that the joy of medical practice comes from the excitement, stimulation, and pleasurable feedback which result from our unique capability to help fellow human beings deal with what, to them, are mysterious health problems. Monetary reward takes second place. Observation during this year as your President reinforces that view and gives me a feeling of pride in my profession.

Good feelings on the part of the physician and his patient are most likely to be present when there is a close personal relationship. I think it will be to society's benefit if health planning proceeds in a manner to emphasize this fact. We must, at all costs, avoid depersonalizing human beings. This is true, not only in medical care, but in all facets of our interpersonal relationship. Physicians may be more aware of this need than any other group. For that reason, they need to be present through their representatives at the forefront of social planning. Such representation is possible in no other way than through organized medicine.

Observation over these past two years allows me to reassure you that your MMA continues to evolve into an increasingly strong and influential organization. In the person of Dr. James Knapp, you have strong, firm and yet gentle, sensitive leadership. Dr. John Meinert, who succeeds to the office of President, is talented, has excellent background experience, and is a demonstrated team player. I am confident that he will exemplify himself in this office. Your trustee representatives and other officers are likewise highly talented, interested, and willing to give of themselves for the organization. The administrative staff cannot help but impress one with its sincere dedication and the energy it expends on behalf of our Association. Its current and long range plans for improving the structure and operation of the Association causes me to be hopeful that we will continue to grow evermore strong and effective in the cause of an improved society and better health for American citizens.

I am indebted to you all for electing me to the office of President. It has been a truly educational experience; one that I have enjoyed and will cherish. Current problems loom large, but that has historically always been true. Organized medicine is today better equipped than ever before to deal with current and future problems. However, to be most effective, we need the help of every eligible person.

I am surprised, as this last letter draws to a close, to experience a feeling of regret. This means, to me, that it has been a pleasant task. Questions are: Will my regret be matched by the readers' relief? Have the letters had any effect? Was the effect good or bad? I suppose that I will never know and perhaps that is just as well.

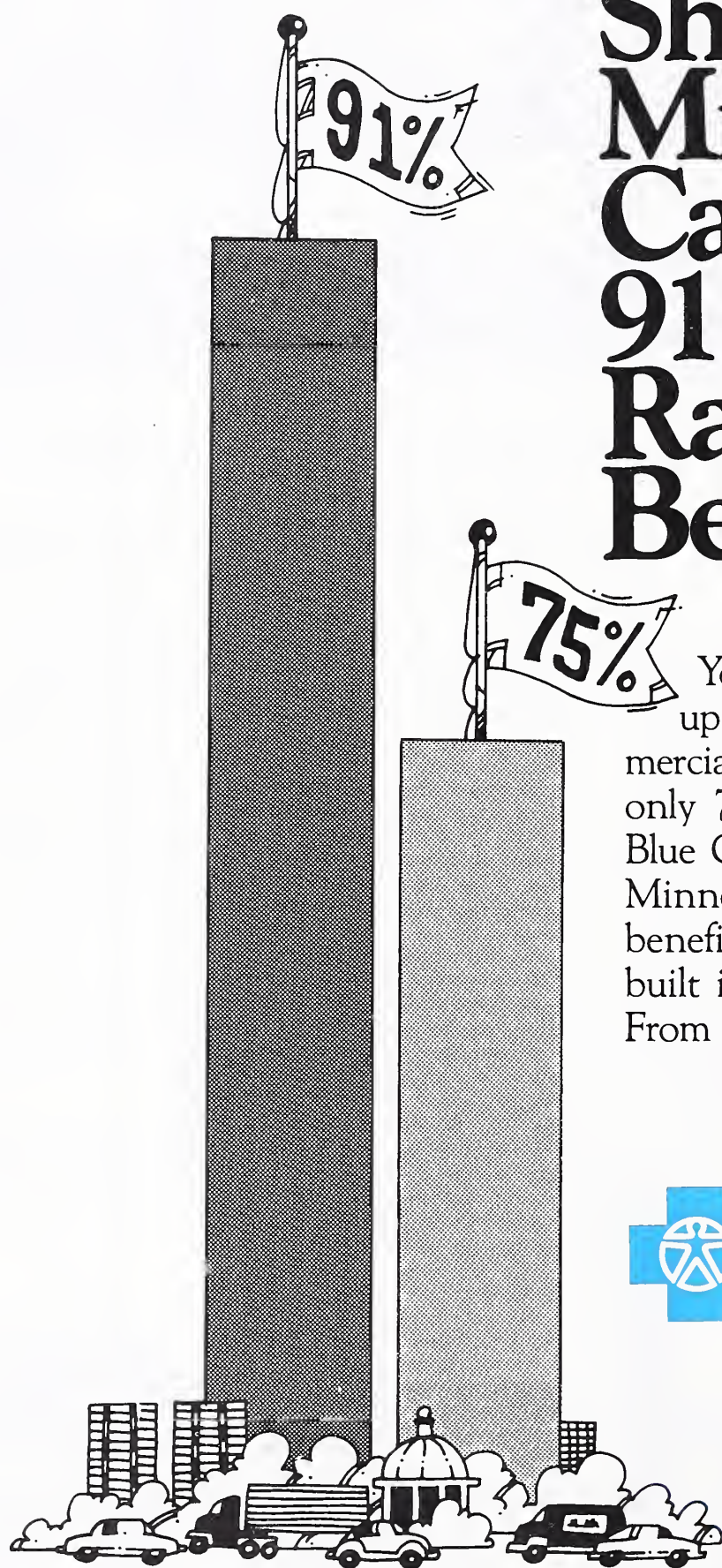


Frank E. Johnson, M.D.  
President  
Minnesota Medical Association

P.S. Not because it is an after thought but rather to emphasize by setting it apart is my expression of sincere thanks to Elaine Nye, Ph.D., Assistant Editor for time and help she has given so generously.



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# Editor's Notebook

## Editor's Report to the House of Delegates

This is my sixth Editor's report. As such, it represents a kind of annual State of the Journal Address. Perhaps "Undress" would be a better term, for each year I reveal our liabilities and assets. What I say here will resemble a miniskirt — short enough to be interesting but long enough to cover the subject matter.

But enough skirting the issue. I shall now get down to basics.

To begin with, 1979 was a good year — editorially, esthetically, and financially.

We continue to receive good manuscripts. For example, one of the award winning papers this year described results of the first 1,000 renal transplants at the University of Minnesota. We had special issues on Diabetes Mellitus, Psychopharmacology, and Medical Oncology. The Minneapolis Children's Hospital also contributed a special issue. Supplements included: Minnesota Cervical Cancer Mortality Study, a Health Care Cost Commission Report, and the membership Roster.

Members continue to deluge us with excellent photographs for use on our covers. Doctor Farrell Stiegler, who has done such an excellent job over the years selecting our covers, will step down at the end of 1980 as our cover editor. Doctor Bruce Nydahl will assume his duties. Bruce, you may remember, contributed the beautiful picture of spring crocuses on the March 1980 cover.

We are proud of our financial performance in 1979. Although printing and mailing expenses mounted by about 15 percent and the general inflation rate was 13 percent, our budget remained essentially stationary. Indeed, as you will note in the accompanying Table, we ended 1979 \$5,813 under budget.

Year	Budget	%Increase (approx.)	Financial Performance	Pages per issue
1975	\$40,000	0%	\$1,163 under budget	76
1976	\$44,000	10%	932 under budget	74
1977	\$46,000	5%	8,010 over budget	75
1978	\$56,000	22%	475 over budget	61
1979	\$60,000	7%	\$5,813 under budget	76

Of course, I would like to attribute this impressive performance to a sharp editorial pencil, a keen managerial eye, and ruthless cost cutting style. Certainly, you must always keep those possibilities firmly in mind. But you are too sophisticated an audience to accept self-applause. So I shall have to confess one large reason for our success is our sustained effort, through a local media representative, to attain more local advertising from banks, luxury car dealers and investment houses. You can better appreciate this effort if you consider the mix of income and expenses through the first three months of 1980.

Here, briefly, are a few bare facts.

Income, first three months of 1980 compared to same period in 1979

1. National advertising, down \$1000
2. Local advertising, up \$5300
3. Classified advertising, up \$800
4. Reprint advertising, up \$230.

Expenses, first three months of 1980 compared to same period in 1979

1. Staff salary, same

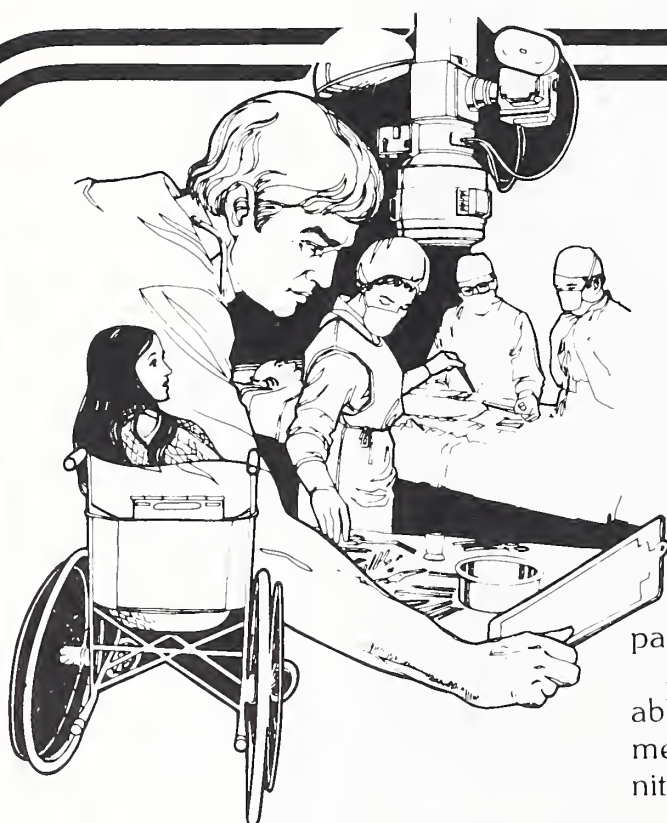


2. Printing expenses, up \$7300
3. Mailing expenses, up \$400
4. Cover photograph expenses, down \$109
5. Editor in chief expense, same
6. Staff expense, up because of increased mileage costs now being applied
7. Local media representative expenses, up but local ads also up
8. State Medical Journal Advertising Commissions down but so are ads

So what does all this forebode for 1980? At this point, I ought to tell you the Finance Committee and I have agreed on a different format for determining the annual budget of *Minnesota Medicine*. We believe this new format is simpler, more understandable, less controversial, and more acceptable to all concerned. The budget will be based on a subscription charge of \$15 per member of the Association. To put it another way, the journal will cost each member \$15 of his annual dues, or \$1.25 a month. The Association now has about 4000 regular active members, so the annual budget for 1980 will be about \$60,000. If membership drops, so will the budget. If the 1980 membership drive succeeds in attracting more members, then our future budgets will increase.

I would like to conclude with a rousing statement about our plans for next year. But I will not. These are uncertain times. So I shall simply close by saying we shall do as well as shifting conditions permit. Thank you for your continuing support.

*Richard L. Reece MD*



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# Candidacy



Robert T. Kelly, M.D.

Dr. Robert T. Kelly, after a long career in medical affairs in the Range County Medical Society, the Minnesota Medical Association, and the AMA, is a candidate for the Board of Trustees of AMA.

Bob has served as an AMA Alternate Delegate and Delegate for twelve years in the House and chaired the MMA delegation. He was elected to the Council on Medical Service in 1974 and was recognized there for his leadership by being elected successively Vice-Chairman and Chairman of that Council. He headed an ad hoc committee on PSRO of the Council. He is a member of the National PSRO Advisory Council; served on the AMA Speaker's Bureau; and chaired the Ad Hoc Committee on Practice Evaluation.

He is former President of the North Central Medical Conference.



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# Case Report

## Serial Gallium-67 Imaging for Localization of Septic Lesions

MATHIS P. FRICK, M.D.\*; KAMALUDDIN AHMED, M.D.\*, and MERLE K. LOKEN, M.D., Ph.D.\*

**Given the appropriate clinical setting, gallium scanning is useful in detecting intraabdominal inflammatory foci. The value of gallium imaging is illustrated by this case report in which two different infectious processes occurring on separate occasions could be demonstrated.**

A 26-YEAR-OLD woman underwent jejunoileal bypass surgery for obesity. During the immediate postoperative period she appeared to do well but gradually lost weight. Fourteen months later, she was readmitted to the hospital because of general weakness and clinical evidence of nutritional deficiency and hepatic failure. A liver biopsy revealed micronodular cirrhosis and mild fatty metamorphosis. A cholecystectomy for cholelithiasis and a jejunostomy to augment nutrition were performed. Postoperatively, the patient exhibited fever and leukocytosis. Total body scans two and four days after administration of 3 mCi of Ga-67 disclosed abnormal accumulation of radioactivity in both kidneys suggesting pyelonephritis, although the IVP was normal (Figure 1A). The diagnosis of pyelonephritis was supported by *positive urinalysis* and *urine culture*. The patient improved clinically on antibiotics and *urinalysis* returned to normal. A repeat Ga-67 scan was normal (Figure 1B).

The patient was readmitted to the hospital three months later with fever and abdominal pain. A superficial abscess was drained from the site of the previous right upper quadrant incision. A fistulogram of the superficial abscess cavity demonstrated no tract into deeper structures. The patient was given various antibiotics, but fever and leukocytosis persisted. A whole body scan at four days after administration of 3 mCi of Ga-67 showed abnormally increased radioactivity in the lower abdomen (Figure 1C, arrows). Subsequently a large abscess was drained from the left lower quadrant. Culture of the pus grew *E. coli*. The patient's condition gradually improved. A subsequent Ga-67 scan was normal.

### Discussion

Gallium-67 citrate is being used for the localization of malignant and inflammatory processes. Gallium is normally accumulated in the liver, spleen and axial skeleton. Biliary excretion occurs after six hours and

\*Department of Radiology, Division of Nuclear Medicine, University of Minnesota, School of Medicine, Minneapolis, Minnesota.

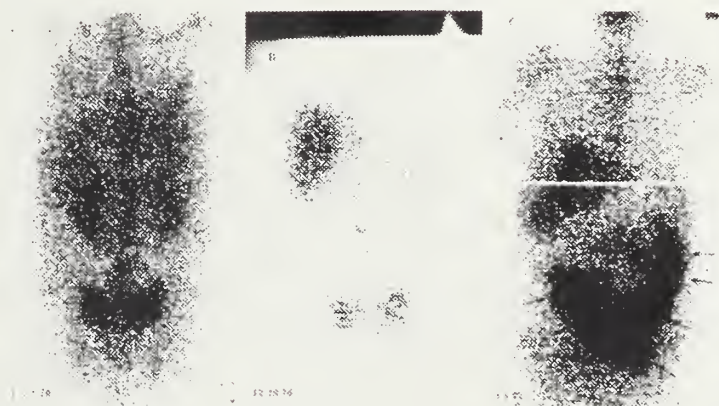
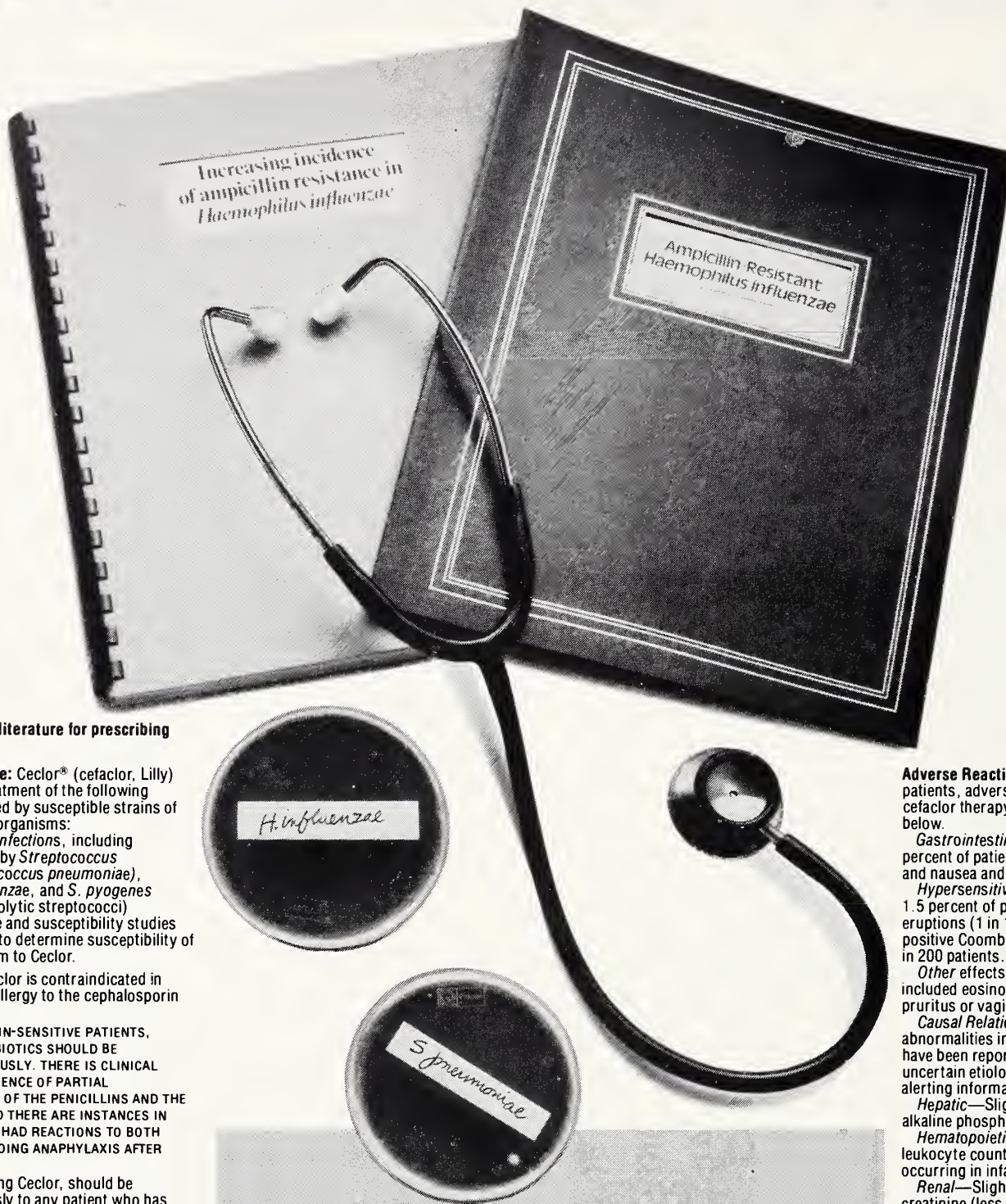


Figure — Abnormal increased 67-Gallium accumulation in both kidneys secondary to pyelonephritis (left:A). Normal 67-Gallium scan after appropriate antibiotic treatment (middle:B). Abnormal increased activity in lower abdomen due to intraabdominal abscess (right:C).



# An added complication... in the treatment of bacterial bronchitis\*



**Brief Summary.**  
Consult the package literature for prescribing information.

**Indications and Usage:** Cefclor® (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

*Lower respiratory infections*, including pneumonia caused by *Streptococcus pneumoniae* (*Diplococcus pneumoniae*), *Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci). Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Cefclor.

**Contraindication:** Cefclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

**Warnings:** IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS TO BOTH DRUG CLASSES (INCLUDING ANAPHYLAXIS AFTER PARENTERAL USE).

Antibiotics, including Cefclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

**Precautions:** If an allergic reaction to cefaclor occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of cefaclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs test may be due to the drug.

Cefclor should be administered with caution in the presence of markedly impaired renal function. Under such a condition, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

**Usage in Pregnancy**—Although no teratogenic or antifertility effects were seen in reproduction studies in mice and rats receiving up to 12 times the maximum human dose or in ferrets given three times the maximum human dose, the safety of this drug for use in human pregnancy has not been established. The benefits of the drug in pregnant women should be weighed against a possible risk to the fetus.

**Usage in Infancy**—Safety of this product for use in infants less than one month of age has not been established.

## Some ampicillin-resistant strains of *Haemophilus influenzae*—a recognized complication of bacterial bronchitis\*—are sensitive to treatment with Cefclor.<sup>1-6</sup>

In clinical trials, patients with bacterial bronchitis due to susceptible strains of *Streptococcus pneumoniae*, *H. influenzae*, *S. pyogenes* (group A beta-hemolytic streptococci), or multiple organisms achieved a satisfactory clinical response with Cefclor.<sup>7</sup>

# Cefclor®

## cefaclor

Pulvules®, 250 and 500 mg

**Adverse Reactions:** In clinical studies in 1493 patients, adverse effects considered related to cefaclor therapy were uncommon and are listed below.

*Gastrointestinal* symptoms occurred in about 2.5 percent of patients and included diarrhea (1 in 70) and nausea and vomiting (1 in 90).

*Hypersensitivity* reactions were reported in about 1.5 percent of patients and included morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs tests each occurred in less than 1 in 200 patients.

*Other* effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

**Causal Relationship Uncertain**—Transitory abnormalities in clinical laboratory tests results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

*Hepatic*—Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

*Hematopoietic*—Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

*Renal*—Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[070379R]

\* Many authorities attribute acute infectious exacerbation of chronic bronchitis to either *S. pneumoniae* or *H. influenzae*.<sup>8</sup>

**Note:** Cefclor® (cefaclor) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

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Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285. Eli Lilly Industries, Inc. Carolina, Puerto Rico 00630

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colon activity after 24 hours or less. Radioactivity in the kidney and bladder usually is seen on the early scan but disappears at 24 hours. Persistent renal accumulation after 24 hours is abnormal, and has been observed in cases of acute and chronic pyelonephritis, acute tubular necrosis, vasculitis<sup>5-7</sup> and neoplasms such as lymphoma.

In patients with fever of unknown origin, gallium imaging has proven useful in detecting underlying inflammatory lesions in the peritoneal and retroperitoneal spaces.<sup>8-15</sup> Its value is illustrated by the case reported above, in which two different infection processes occurring on separate occasions were demonstrated.

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#### Continuing Medical Education

University of Health Sciences/The Chicago Medical School announces a symposium on "Changing Concepts in Trauma Care" on Saturday, June 7, 1980, at the Marriott Lincolnshire Resort, Lincolnshire, Illinois. A distinguished faculty from leading universities in the country will participate in the symposium. Ample time for pre-and post tests and question and answer sessions has been allotted. Registration fee: Physicians-\$100, residents-in-training, nurses, paramedics-\$50, including a luncheon with the faculty. For further information call Miss Christine Chiaramonte at 312-770-2243 or-2369, or Dr. Sriram at 312-770-2000 or write to Miss Chiaramonte at Saint Mary of Nazareth Hospital, Room 1043, 2233 West Division Street, Chicago, Illinois 60622.

#### MINNPAC Will Canvass the State this Summer and Fall

Dr. Lloyd "Ash" Whitesell, Chairman of your MINNPAC Board, reports that your MINNPAC Board will be canvassing the state this summer and fall in an attempt to *inform the medical community of the importance of the 1980 fall election*. "The upcoming elections are *critical to medicine*," said Dr. Whitesell, noting that the persons elected this fall will have a significant role in fashioning legislation for the decade.

Dr. Whitesell encourages *each of you to get involved and* to call your MINNPAC office at (612) 227-1342 if you need further information or would like to share concerns. He is especially pleased that many Auxilians are actively participating in MINNPAC.

"The only distressing news to report is that MINNPAC membership is down," said Dr. Whitesell, adding that if membership doesn't increase, *organized medicine* will have little to contribute to worthy candidates. Your MINNPAC Board is now working on new ways to stimulate MINNPAC membership and it invites your recommendations.



# Disc Space Infection in Children, Late Adolescents, and Adults\*

LEO J. De SOUZA, M.B., F.R.C.S. (EDIN), F.R.C.S. (C)†

Intervertebral disc space infection is a relatively uncommon entity. Nonetheless, awareness of the possibility of the disorder is the key to management. This paper discusses the classical and some unusual presentations of disc space infection in children and contrasts these with the findings in adolescents and adults. Four illustrative case reports are included.

**A**LTHOUGH OSTEOMYELITIS of the spine may be uncommon, it is certainly a well-known condition. While disc space infection is not any more uncommon than osteomyelitis of the spine, it remains to this day a relatively unrecognized entity. Quite often, therefore, it goes unsuspected and undiagnosed when it first presents itself to the primary physician.

Disk space infection has been a recognized entity in children since at least 1950<sup>1</sup> and the first case was probably described 50 years ago by Mayer<sup>2</sup> when he illustrated the difference between kyphosis from disc loss and kyphosis from vertebral body destruction. Bonfiglio et al<sup>3</sup> reported in 1973 that they saw three or four cases per year for all ages at the University of Iowa Hospitals; our incidence at the St. Louis Park Medical Center is two or three cases per year, and the cases seen since October of 1974 are included in the Table.

\*Based on a paper read at the course on orthopedic problems for Family Practice and Emergency Medicine Physicians at the Hennepin County Medical Center, September/October 1977.

†Department of Orthopedic Surgery, St. Louis Park Medical Center, Minneapolis, and attending staff, Department of Orthopedic Surgery, Hennepin County Medical Center, Minneapolis.

## Infections in Children

The child classically presents between the ages of two and ten with pain in the back of one to two weeks' duration. The backache is localized around the involved vertebral area, which usually is lumbar, although the pain may radiate into the buttock, hip, leg, or abdomen. If the child walks, a limp usually is present. Usually, however, the child refuses to sit, stand or walk and is not acutely ill but is irritable and prefers a recumbent position. The temperature is elevated but rarely above 101° F.

The principal physical finding is paravertebral muscle spasm. The lumbar lordosis usually is lost. Hamstring muscle spasm may be present and, if so, straight leg raising will be limited. Tenderness at the site of the lesion will be present and spine compression induced by striking the heel or the head will elicit pain at the involved site.

About half the cases will present in this classic manner with symptoms and signs mainly in the back. In the others, the presenting symptoms may be pain in the hip region or the lower extremity or both.

TABLE  
Disc Space Infection:  
Age, Sex, Site of Involvement, and Organisms Cultured  
in Eight Patients Seen Since October 1974.

Case	Age	Sex	Level	Organism obtained from biopsy (aspiration) of the disc space
1	3	F	L5/S1	None, but aspirate contained moderate numbers of polymorphonuclear leukocytes
2	4	M	L4/L5	Staphylococci, coagulase-positive
3	16	F	L1/L2	Staphylococci, coagulase-positive
4	33	F	L4/L5	Staphylococci, coagulase-positive
5	47	F	T8/T9	Staphylococci, coagulase-positive
6	71	F	T10/T11	None, but nonspecific inflammatory process was found in fibrocartilage at biopsy
7	76	F	T11/T12	<i>Bacteroides fragilis</i>
8	80	M	L3/L4	Enterococci



Sometimes the main complaints may be pain in the abdomen, anorexia, and occasionally vomiting and ileus. Not infrequently the child will present with just irritability associated with meningeal infection. Rocco and Eyring<sup>4</sup> on reviewing 150 cases collected from the literature and their own records found that about half of these children presented with back pain and about one-fourth had hip or leg pain.

Once disc space infection is suspected, laboratory investigations should include CBC and sedimentation rate, blood, throat and urine cultures, agglutination tests (Widal and brucella), TB skin test, chest Xray, and cerebrospinal fluid examination. The sedimentation rate is raised in about 85% of the cases and usually is in the 50 to 60 mm range. The WBC may be normal, and the blood cultures may be positive. However, plain roentgenograms of the affected area of the spine often are of great help in diagnosing and localizing the lesion, and bone scans and laminograms are valuable secondary procedures. Disc space narrowing is the first radiological sign, usually noted three weeks after the onset of symptoms. Narrowing is soon followed by end plate haziness, irregularity, and erosion. The bone scan shows a localized area of increased radionuclide concentration in the affected portion of the spine. It is invariably positive and precedes the radiological findings. The bacterial or infective diagnosis is made by needle aspiration of the affected space performed ideally under image intensifier control. If no pus or aspirate is obtained, 1 or 2 ml. of saline are injected and then reaspirated for culture and sensitivity studies.

The most important part of treatment is rest, and the spine is best rested in a body cast. The period of immobilization is continued until back pain, muscle spasm, and local tenderness have subsided, until the sedimentation rate is down to normal limits, and until the roentgenograms indicate that no further bony destruction is taking place. This normally takes two to three months, following which the spine usually is protected in a brace for one to two months. Antibiotics usually or almost always are given on the basis that the disc space lesion is the result of hematogenous infection. In those cases in which the organism is cultured either from the disc space or from the blood and sensitivities known, the selection of the appropriate antibiotic is no problem. In those cases where no organism has been obtained, the empirical selection of antibiotics is based on the fact that *Staphylococcus aureus*, coagulase-positive, is the most commonly isolated organism. The antibiotic therefore most often chosen is an antistaphylococcal penicillin. In children

aged three and under, ampicillin would be added to cover the possibility of infection by *Hemophilus influenzae*. Antibiotics are continued until the temperature is down, pain has subsided, sedimentation rate is normal, and radiological healing is in progress. This usually takes a few weeks to a few months.

As mentioned earlier, the etiology of this condition is believed to be a hematogenous infection. There is no doubt about this pathogenesis when an organism is isolated and cultured from the affected disc space. However, the mild clinical signs and symptoms, the infrequency of positive cultures for organisms, being positive only in about one-third of the cases, the nonspecific changes on tissue examination, and the favorable response without antibiotics, have led many to believe that we may not be dealing with an infective lesion.

It is believed that the disc space may respond to different insults, traumatic, infective, or both, by the same radiological appearance of narrowing. Antibiotics are, therefore, not used universally and in some centers antibiotics will be administered only if specific indications exist, such as a positive biopsy or blood culture, clinical progression in spite of adequate immobilization, and recurrence of back pain accompanied by an increased sedimentation rate, white cell count, and an elevated temperature.<sup>5</sup>

Surgery is seldom indicated in children.

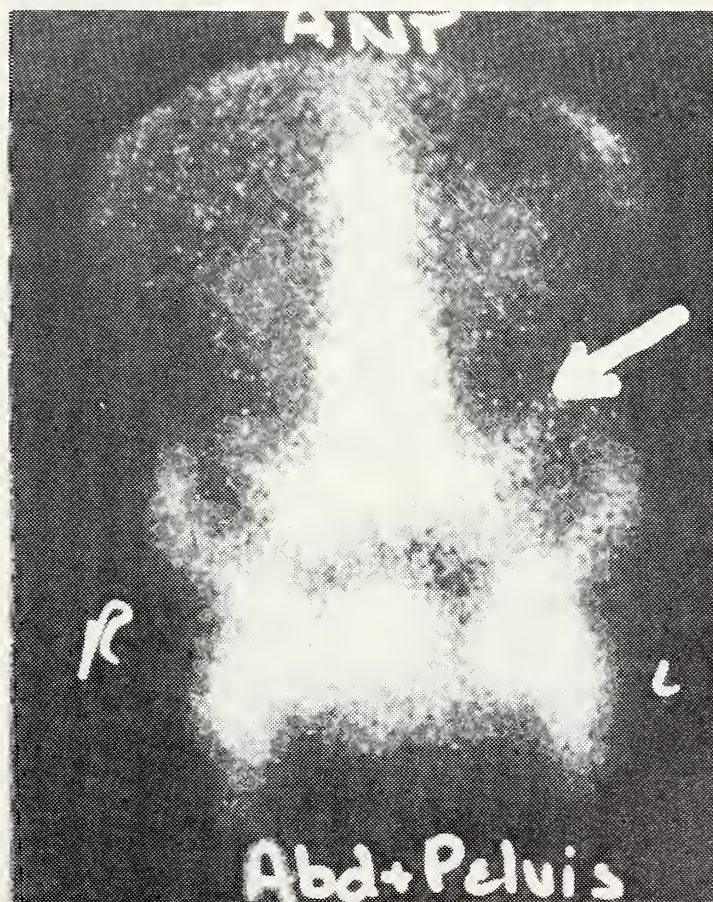


Fig. 1(A) — A bone scan showing increased isotopic concentration in L4/L5 vertebral region.



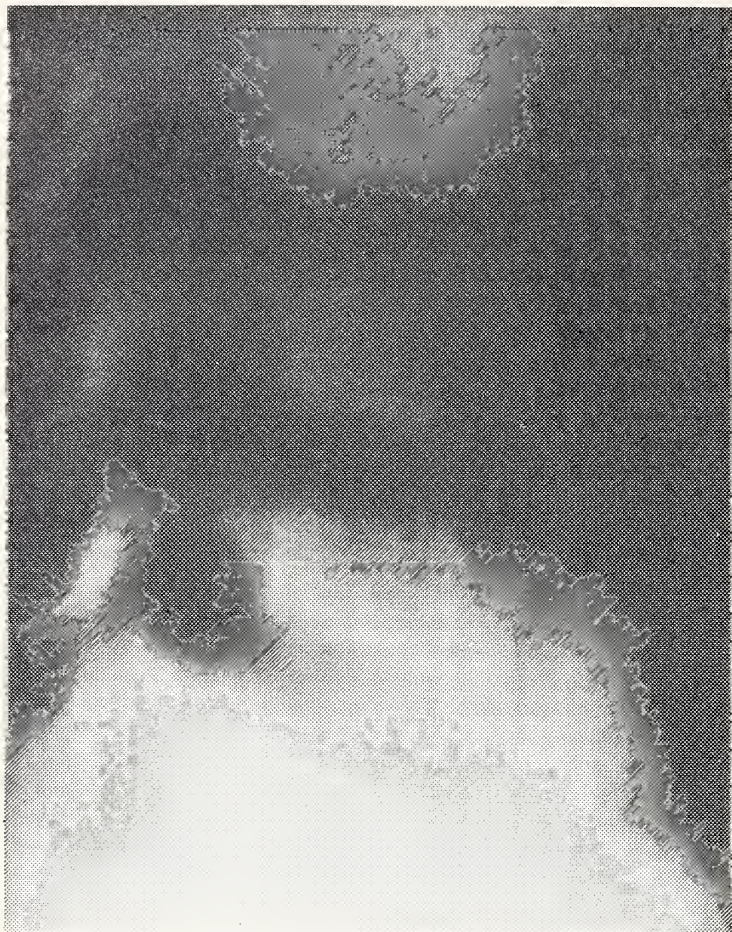


Fig. 1(B) — A planogram of Case 1 showing narrowing of the L4/L5 disc space with haziness of the end plates.

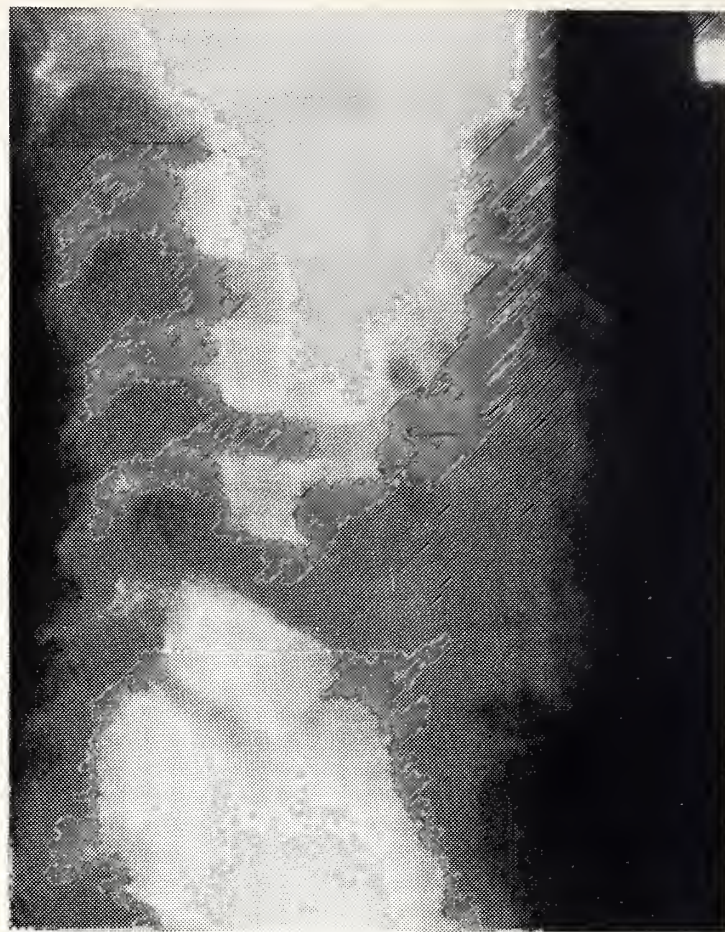
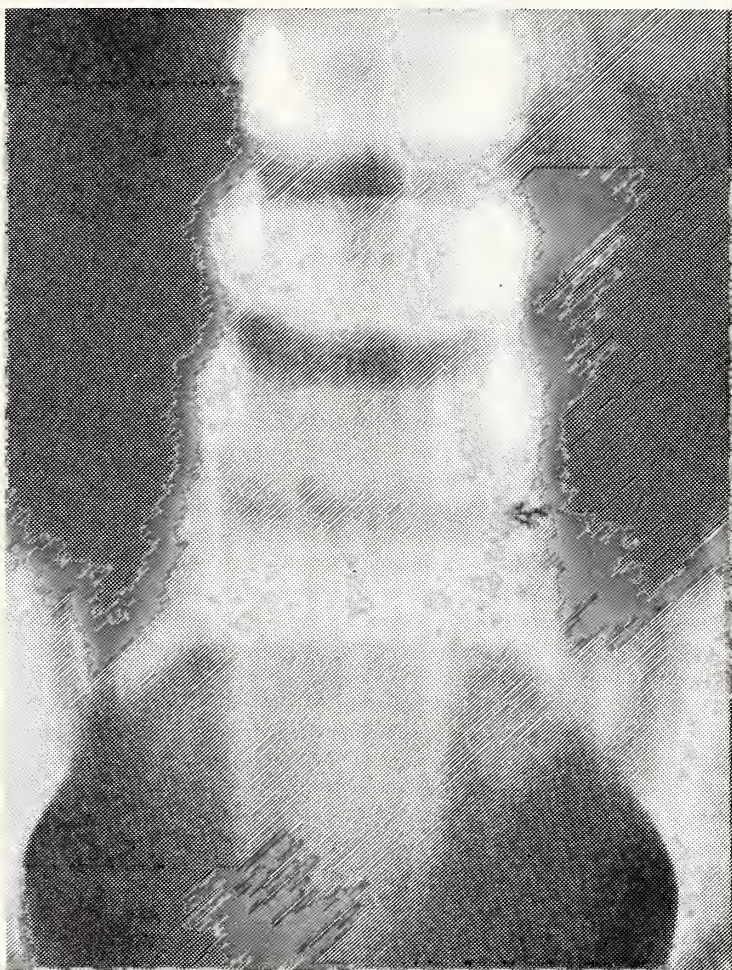


Fig 1(C) — A lateral roentgenogram a year after treatment. Recovery is complete, but narrowing of the L4/L5 disc space persists.



Figs. 2 (A.-left) and 2 (B-right) — Roentgenograms (AP and lat.) showing narrowing of L 5/S1 disc space with haziness of the end plates.



## Case Reports of Children

### Case 1 (classical presentation)

A four-year-old male child was admitted with low back pain of three weeks' duration. The pain had become increasingly severe, so that at the time of admission, the child refused to stand or walk. Sitting was also uncomfortable, so he lay in bed all the time. One week before the onset of low back pain, the child had an episode of upper respiratory infection.

Examination revealed an irritable child with a temperature of 100° F. Lumbar lordosis was obliterated and there was marked paravertebral muscle spasm. Hamstring muscle spasm also was present, with the result that the straight leg raising test was restricted to 20° bilaterally. There also was tenderness in the mid-lumbar region. No neurological abnormality was noted, the abdomen was soft, and the hips were normal.

Roentgenograms of the lumbar spine at admission were negative. The CBC was normal, but the ESR was elevated to 55 mm. Blood and urine cultures were negative, as were agglutination and skin tests. The myelogram was normal, and so was the CSF. The bone scan using technetium 99m labeled to pyrophosphate done a week after admission showed an area of increased isotopic concentration in the lower lumbar region (Figure 1A), and the planograms showed narrowing of the L4/L5 disc space with haziness of the end plates (Figure 1B). At this stage a tentative diagnosis of disc space infection was made. Needle aspiration biopsy was carried out; no frank pus was obtained, but coagulase-positive staphylococcal organisms were cultured and proved to be sensitive to penicillin.

The child was initially treated with methicillin and ampicillin, which was changed to penicillin after the sensitivities were obtained. He was also placed in a body cast with a bilateral hip spica, which was kept for two months. The antibiotics were continued for three months. Figure 1C shows his Xray film a year after treatment. The child made a complete recovery, but the L4/L5 disc space has remained narrowed.

### Case 2 (atypical presentation)

A three-year-old girl was admitted with a 48-hour history of increasing pain referred to the lower abdomen. The first three days in the hospital were spent investigating abdominal pathology. She was seen by the general surgery department, and plain films of the abdomen were obtained, a barium enema was performed, and an IVP was carried out. On the fourth day it became apparent that the pain was located in the lower back. Lumbar spine films were normal, but a bone scan using technetium 99m labeled to methylene diphosphate showed an abnormal focal lesion in the lower lumbar spine. Planograms showed narrowing of the L5/S1 disc space with haziness (Figures 2A and 2B). Needle aspirate drew no pus and grew no organisms, but polymorphonuclear leukocytes were seen. The child was started on methicillin and ampicillin therapy and the spine immobilized in a body cast with bilateral hip spica for two months. Recovery was complete. Figure 2C shows healing at four months with residual disc space narrowing.

## Infection in Late Adolescents and Adults

The disc space in children is amply supplied by blood vessels; youngsters therefore are amply exposed to infectious agents carried in the blood stream. These vascular channels in the discs, however, undergo degeneration early in life, disappearing between the ages of 20 and 30. The normal adult disc is therefore considered to be avascular. If this were totally true, no disc space infection would be seen in the late adolescent and in the adult. However, infections are

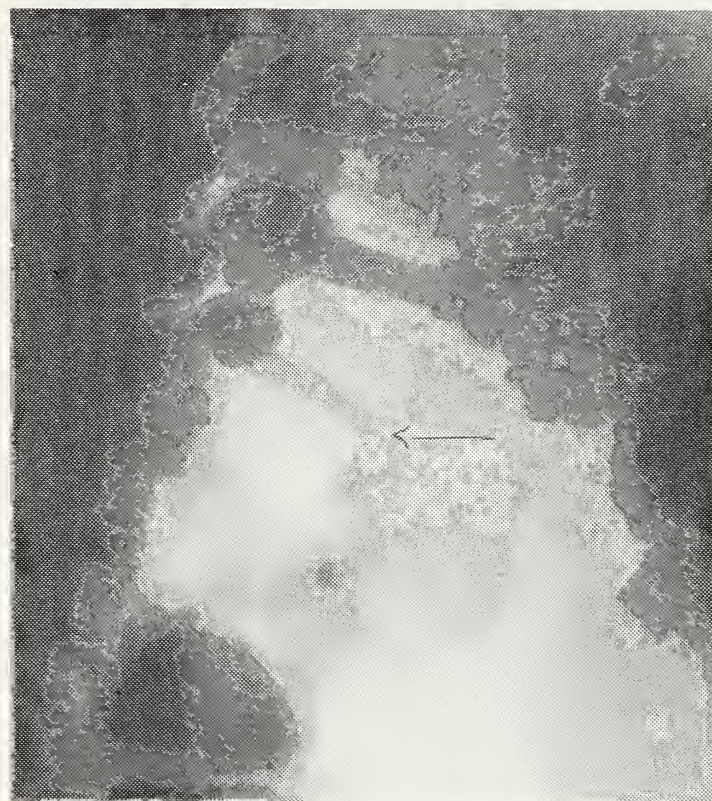


Fig 2(C) — A lateral roentgenogram four months following treatment, showing healing with residual disc space narrowing.

encountered in older patients, although not as frequently as in children. As a matter of fact, Wiley and Trueta<sup>5</sup> and subsequently others<sup>7,8</sup> have shown that although the blood supply to the discs diminishes with age because of decrease in the number of vessels that enter the nucleus pulposus from the adjacent vertebrae, an adequate circumferential supply is maintained from the periphery.

Kemp et al<sup>9</sup> reported from the Royal National Orthopedic Hospital, London, that they saw between two and three cases each year. The patients all complain of back pain, which they can localize accurately. Almost all patients with lesions in the lumbar spine have referred pain of femoral or sciatic distribution, and all exhibit local tenderness, paravertebral muscle spasm, and limitation of motion.

The earliest radiological sign is narrowing of the affected disc space; this is followed by progressive sclerosis of the subchondral bone and then by progressive irregularity of the adjacent vertebral plates from erosion. About half of the cases do not progress beyond this stage; those that do show extension or erosion into the vertebral bodies with characteristic ballooning of the disc space.

The adults differ from the children in many ways. First, the adult lesion exhibits a chronicity that is not observed in children. Second, the diagnosis usually is delayed in most patients, the average period between the onset of the symptoms and the establishment of the diagnosis being six months. This probably is related to failure to recognize the radiological signs of the lesion; in addition, the investigations are of little assistance, and the needle biopsy helpful in only about one-third of the patients.

The Craig needle<sup>10</sup> usually is used for the biopsy, although the Ottolenghi needle<sup>11</sup> with bar and guide makes for greater technical ease. The disc spaces in the lumbar spine are more easily accessible, and greater apprehension exists with needling the thoracic disc space for fear of puncturing the pleura or lung. This is avoided by placing the site of needle entry medial to the angle of the rib, observing the correct angle of insertion and if a rib is encountered by manipulating the needle to pass superior to the rib. Occasionally open biopsy might



be indicated, using the limited procedure of costotransversectomy or the anterior spinal approach which can be combined with the definitive treatment.<sup>12</sup> The one test that is consistently helpful is the bone scan.

In the intravenous "drug" user, pseudomonas is emerging, particularly on the West Coast, as the commonest organism,<sup>13</sup> although in the Midwest coagulase-positive staphylococci continue to be the predominant causative organism in adolescents, regardless of whether or not they use drugs. The sedimentation rate is not a reliable guide in monitoring the progress because of concomitant liver involvement in the "drug" user. In the adult patient, gram-negative organisms are more often encountered due to a primary urinary tract infection or subsequent to surgical instrumentation. Disc space infection following disc excision is not included in this discussion, as it constitutes a totally different entity.

The incidence of disc space infection is probably greater in the adolescent diabetic.<sup>3</sup> Furthermore, in the older patients the most serious feature is the high incidence of spinal cord involvement, which ranges from 15 to 40% according to different sources.<sup>3,9,12</sup>

The present management of this condition varies a great deal, which is not surprising considering that this is a relatively uncommon condition. Conservative therapy consisting of antibiotics and spinal immobilization remains the sheath-anchor of treatment. This is especially justified in patients with localized lesions, if the causative organism can be identified by needle biopsy or blood culture, particularly when the surgical exploration may be technically

difficult or the patient a poor risk. However, with the work of Hodgson in Hong Kong,<sup>12</sup> the management nowadays is more slanted towards a surgical clearance of the affected disc space. In addition, this allows for definite identification of the organism and sensitivity tests in every case. From the wide experience gained in the field of tuberculosis of the spine, an anterior approach to the affected disc is employed by Hodgson, and this is gaining acceptance in many major centers.<sup>14</sup> In the presence of impending or recently established paraplegia, the surgical procedure is mandatory and should be carried out as an emergency procedure.

## Case Reports of Adults

### Case 1

An 80-year-old man was admitted with severe low back pain. He had had low back pain of varying intensity for six months and was thoroughly investigated in Florida where he was vacationing. Examination revealed only tenderness in the lumbar spine with no definite diagnosis.

When the roentgenograms taken a few months before admission were studied, nondescript narrowing and irregularity of the L4/L5 space was detected, and planograms taken at the time of admission showed ballooning of the disc (Figure 3A). A needle biopsy aspiration of the affected space grew enterococci, sensitive to erythromycin. The patient was placed on the antibiotic, and roentgenograms taken three months later showed satisfactory healing taking place (Figure 3B). The patient was symptom-free at

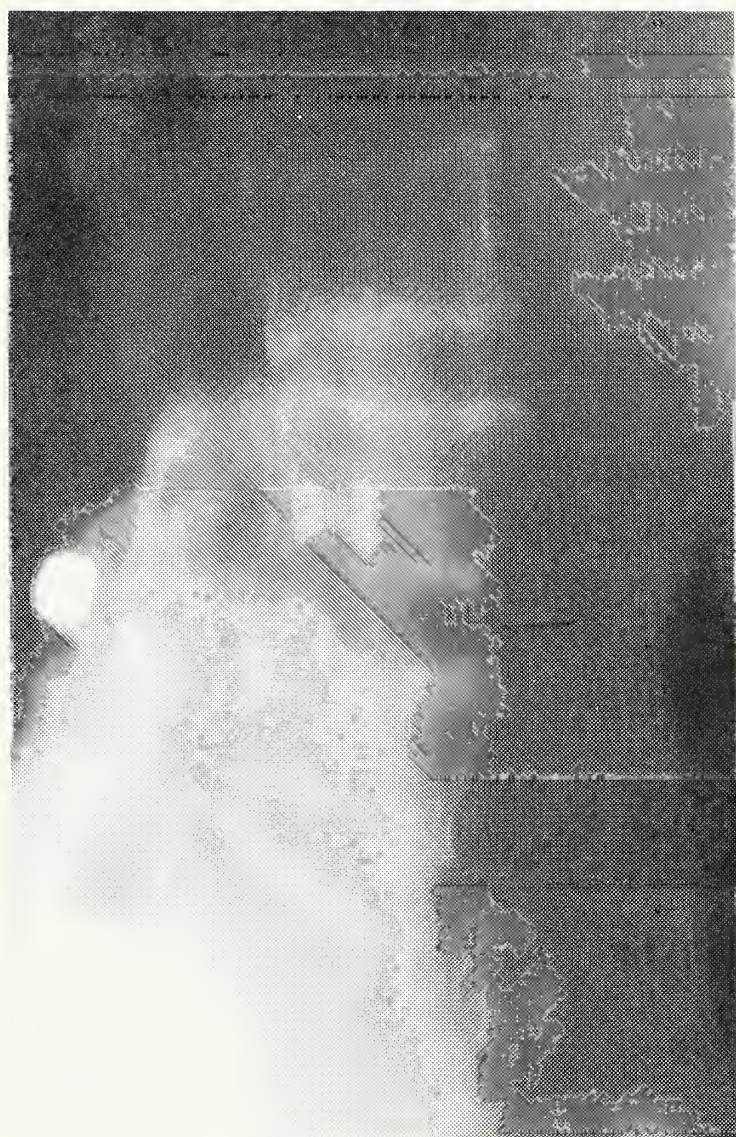


Fig 3(A) — Lateral planogram showing ballooning of L4/L5 disc space.

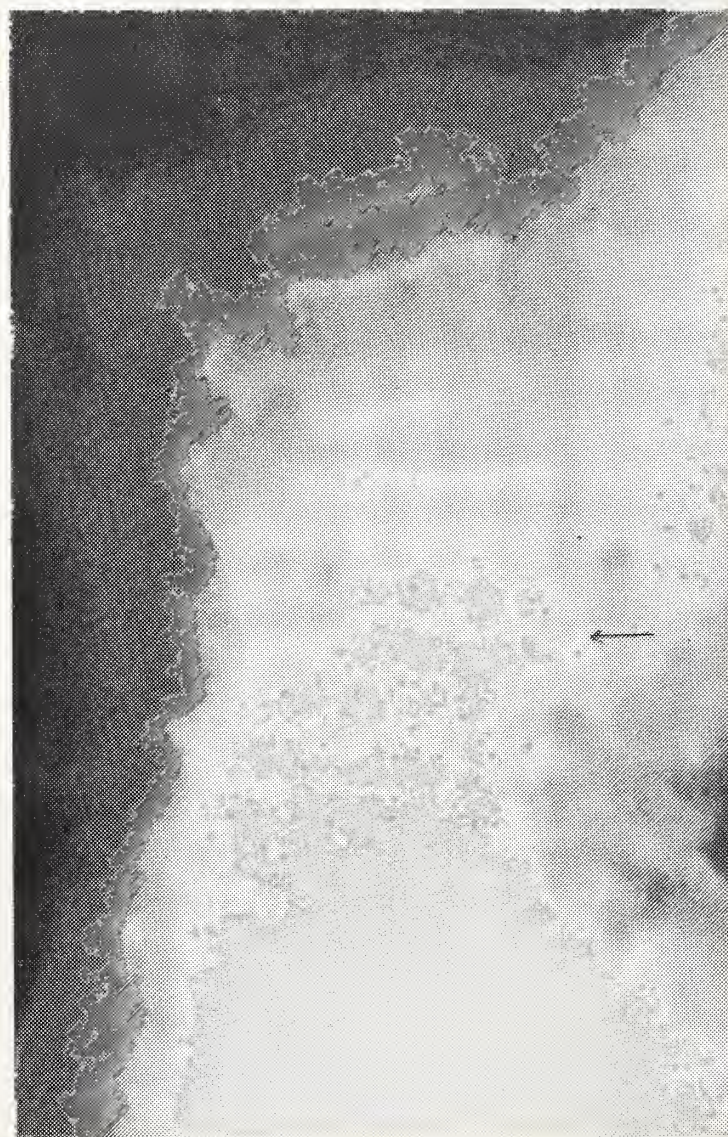


Fig 3(B) — Lateral roentgenogram with healing of affected disc. Note new bone laid down anteriorly.



this stage and refused any further antibiotics. He has also refused any form of immobilization including a brace. When seen a year later he was keeping well and free of pain.

#### Case 2

A 33-year-old woman was admitted with a history of low back pain of two weeks' duration and fever of one week's duration. The pain radiated down both thighs and calves, and the patient also complained of weakness in the legs and of difficulty in walking.

Examination revealed tenderness in the lower lumbar region, with limitation of straight leg raising to 40° bilaterally. There was marked weakness of the ankle dorsiflexors and extensor hallucis longus on both sides. The ankle reflexes were absent bilaterally also.

Lumbar spine roentgenograms were normal, but a myelogram showed an extradural block at the L3/L4 level (Figure 4A), and the bone scan using technetium 99m labeled to stannous pyrophosphate showed an increased isotopic concentration in the lower lumbar region. The planograms showed narrowing of the L4/L5 disc space with haziness of the inferior vertebral plate (Figure 4B). The sedimentation rate was 75 mm per hour and blood cultures grew coagulase-positive staphylococci.

Surgery was performed two days later when a lumbar laminectomy was carried out. Pus was encountered opposite the L4/L5 disc. The disc itself was soft and bulging but was not entered into. After clearance and irrigation the wound was closed.

After initial improvement, the temperature was elevated again. The sedimentation rate rose steadily and lateral planograms two



Fig 4(B) — Planogram demonstrating narrowing of L4/L5 disc space with haziness of inferior vertebral plate.

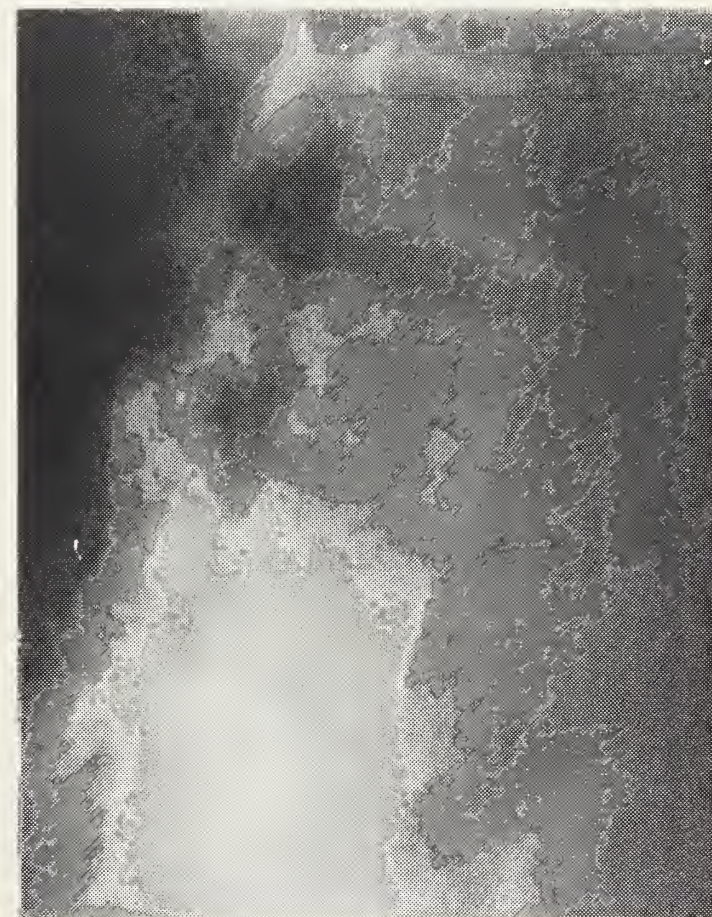


Fig 4(C) — Planogram showing progressing destruction at same disc level.

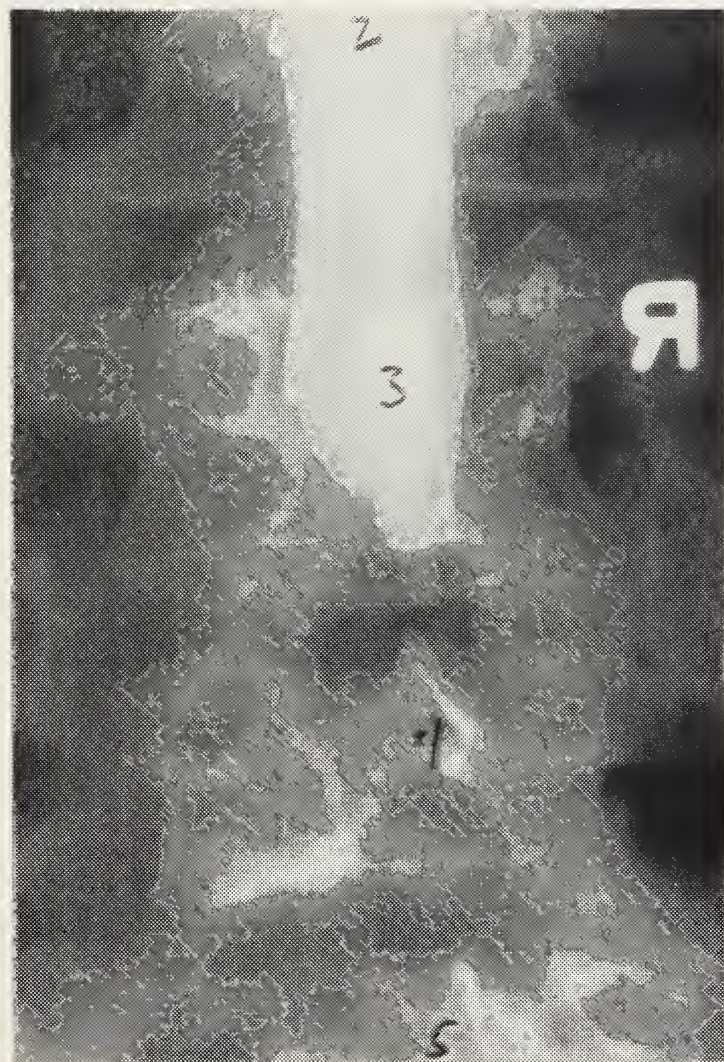


Fig 4(A) — Myelogram showing an extradural block proximal to L3/L4 disc.



weeks later showed a progressive destruction of the adjacent surfaces of the vertebrae (Figure 4C). The back was re-explored and the disc space cleared through the previous approach. The patient made steady improvement thereafter. She was placed in a body cast for three months and in a lumbosacral brace for a similar period. Antibiotics were administered for six months. A year after treatment, there was circumferential fusion across the involved disc space (Figure 4D), and she did recover almost full power in her ankle dorsiflexors.

In retrospect, her recovery might have been faster and probably complete if the affected disc had been cleared at the first surgical intervention, and a complete clearance without fear of endangering the cauda and nerve roots would have been insured by an anterior approach to the disc.

In conclusion, it would be true to say that the management of disc space infection has become fairly standard once it is diagnosed, but to diagnose it one needs to be aware of this very specific entity.

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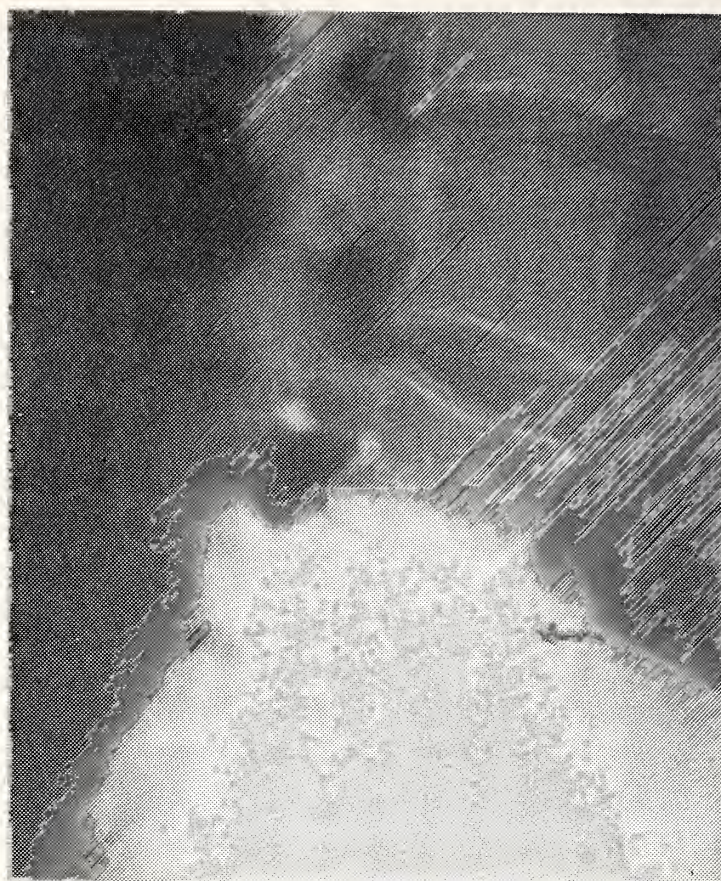


Fig 4(D) — Roentgenogram showing fusion at L4/L5 level a year later.

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# Morphologic Characterization of Long-Term Pancreatic Islet Transplants in Diabetic Rats

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Diabetes in the rat induced by streptozotocin can be reversed by the transplantation of isogenic islets of Langerhans' from neonatal donors. This article describes the morphological characteristics of intraportally transplanted islets studied with the immunoperoxidase staining technique to identify insulin, glucagon, somatostatin and pancreatic polypeptide-containing cells at different times after the transplant. The results of this study establish conclusively that all the known rat pancreatic islet cell types survive and continue functioning long after the transplant and support the theory that islet transplantation may well represent the most physiologic replacement of hormonal deficiencies in the diabetic recipient.

**I**NSULIN DISCOVERY in 1921 and its clinical application was hailed as a cure for diabetes. Insulin prevented death from coma and controlled overt symptoms. However, as the life expectancy of diabetics increased, so did renal, ocular, and cardiovascular lesions of long term diabetes. Because of these complications, the life expectancy of diabetics is still one-third less than the general population. Diabetes is the leading cause of blindness in the United States. Its economic impact in this country is estimated to be more than five billion dollars per year and is expected to double every eight years.<sup>1</sup>

Why diabetes lends to systemic complications is unclear. Evidence supports the view that they result from disordered carbohydrate metabolism secondary to pancreatic islets insufficiency. If this is correct, it may be possible to prevent or treat these lesions through controlling carbohydrate metabolism. This has been attempted in experimental animals using whole pancreas transplants, islet cell transplants, and

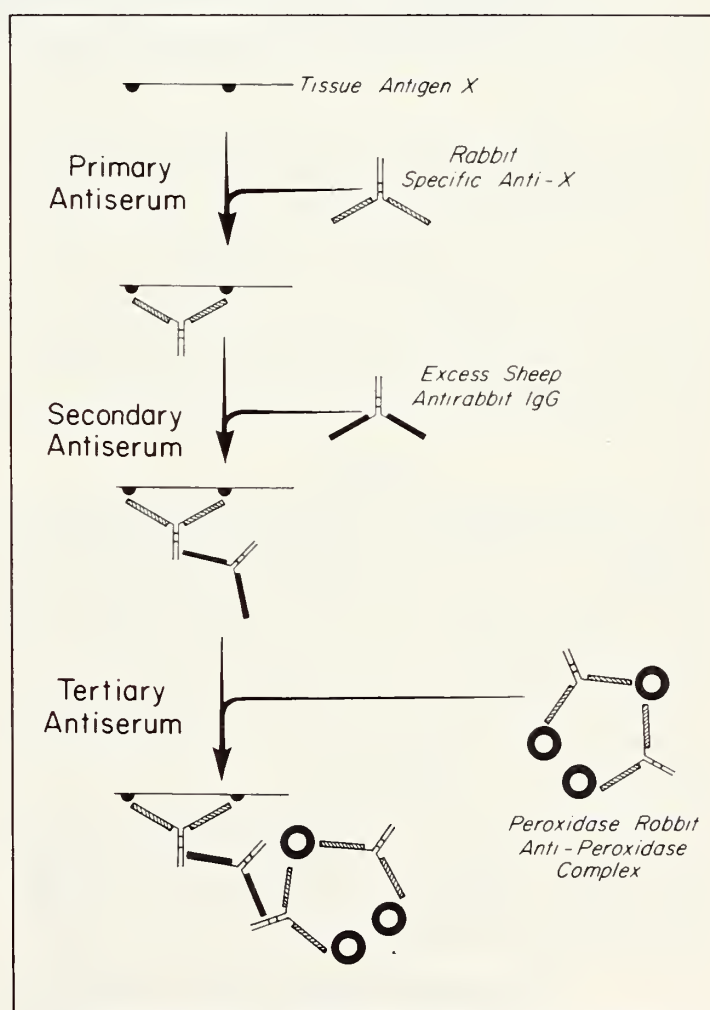


Fig. 1 — The immunoperoxidase technique is accomplished by the sequential addition of antisera resulting in the attachment of the enzyme peroxidase to the antigen (hormone) under study. The brown reaction product is formed from the addition of hydrogen peroxide and 3,3'-diaminobenzidine (sigma) to the tissue. (see text)

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The 1977 Ernst Award Lecture on Anatomic Pathology. The annual Ernst Award for outstanding work in Anatomic Pathology by medical students, graduate students, and residents at the University of Minnesota was established in 1977 in honor of Dr. Kenneth F. Ernst through the generosity of Mr. and Mrs. Thomas R. Turner of Clearwater, Fla., and is administered by the Minnesota Medical Foundation and the Bell Institute of Pathology. James C. Grotting, M.D., was the 1977 awardee.



various implantable insulin delivery systems. These approaches are based on the rationale that new lesion development, or progression of established systemic lesions, will be prevented by precisely regulating carbohydrate metabolism. Insulin does not achieve this degree of control. Diabetics, even when in good control, have wide plasma glucose level swings, whereas normal individuals control plasma glucose within an extraordinarily narrow range.<sup>2,3</sup> Each experimental approach has inherent problems, and none is available for widespread clinical use to date.

Techniques for transplanting pancreatic islets have been developed over the past several years. This method controls experimental diabetes in inbred strains of rats. The team headed by Leonard et al. at the University of Minnesota pioneered methods in our laboratory and demonstrated neonatal rat pancreata could be simply dispersed and transplanted without isolating specific islets.<sup>4,5,6</sup>

Although neonatal islet tissue has been transplanted to such recipient sites as renal capsule, peritoneal cavity, thoracic cavity, and spleen, the liver has certain recipient site advantages such as a rich blood supply and certain physiologic advantages of the hepatic environment.<sup>7,8,9</sup> Matas et al.<sup>10</sup> have reversed experimental diabetes in rats by injecting islet tissue intraportally from one neonatal donor animal. With new methods for identifying specific islet cells types by hormone products, it is now possible to understand the fate of intraportally transplanted islets in diabetic rats. This information is important if we are to fully appreciate how the various islet cells types relate to each other, and the significance of this interplay in carbohydrate metabolism.

Methods

The experimental rat model of diabetes and transplantation technique have been described in detail elsewhere.<sup>11,12</sup> Briefly, diabetes was induced in 14 inbred female Lewis rats (wt. 180-225 gms.) by injecting 50 mg/kg of streptozotocin, a specific beta cell toxin. Diabetes was confirmed by the repeated demonstration of glycosuria and hyperglycemia (plasma glucose > 400 mg/dl).

Pancreata were removed from six to eight day old inbred Lewis neonates. They were finely minced, digested with collagenase, and divided into aliquots containing islets collected from seven donor neonates.

Twelve animals received the islet preparation which was embolized to the liver via a mesenteric vein. Two animals were left as diabetic controls. The animals were sacrificed according to the schedule outlined in the Table.

Histology and Immunohistochemistry

Livers from the recipient animals as well as pancreata from the diabetic controls were screened for islets by staining with hematoxylin-eosin and aldehyde-fuchsin.<sup>13</sup> Specific staining for insulin, glucagon, somatostatin, and pancreatic polypeptide (PP) was accomplished using the unlabeled antibody enzyme technique of Sternberger<sup>14</sup> as modified by Erlandsen.<sup>15</sup> This technique requires three different antisera for the attachment of an antibody-enzyme complex to the hormone under study (Figure 1).

In the first step, the primary antiserum, which consists of a specific rabbit antibody against the hormone (e.g. anti-insulin, anti-glucagon, etc.), is applied to the tissue section. The secondary antiserum, which is a non-specific anti-rabbit IgG made in an unrelated species, e.g. sheep, is then added in excess so that one combining site attaches to the primary antiserum and the other valence is free to bind the antibody enzyme complex.

The antibody-enzyme complex (tertiary antiserum) in the Sternberger method is composed of the enzyme peroxidase covalently bound to a rabbit anti-peroxidase. In this way the peroxidase enzyme is coupled to the hormone in the tissue via a chain of antibodies. Diaminobenzidine and hydrogen peroxide are then added and this results in a brown reaction product visible with the light microscope. By varying the specific primary antiserum, each islet cell type can be identified according to the hormone it produces. Specificity and sensitivity controls for the immunocytochemical stains were performed according to Sternberger's recommendations.<sup>16</sup>

Results

All animals that received streptozotocin became diabetic by our criteria. Similarly, all animals except one that received intraportal islet cell transplants became normoglycemic (plasma glucose < 150 mg/dl) between one and nine days post transplant. All animals began to gain weight, and the plasma insulin levels rose significantly. One animal that was sacrificed at 48

TABLE  
Transplant Recipients

Interval Post Transplant	24 hrs	48 hrs	1wk	2 wks	4 wks	39 wks	65 wks
No of Animals	2	2	2	2	2	1	1



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hours post transplant retained an elevated fasting blood sugar although this was only one-half of the pretransplant value.

#### *Morphology of Dispersed Neonatal Pancreas*

After mincing and collagenase digestion, the neonatal islet preparation consisted of about 80% acinar and ductal elements and 20% islet tissue. Most islets varied in diameter but remained morphologically intact. By immunoperoxidase staining, they were composed of a central core of large numbers of insulin-containing cells and bordered by a peripheral rim of glucagon positive cells. Fewer numbers of somatostatin and PP positive cells were identified in a more intermediate distribution.

#### *Morphologic Appearance of Livers Early Post Transplant*

Numerous islets and acinar fragments could be seen throughout the liver, most of which had lodged in terminal portal vein radicles with some filtering through to hepatic sinusoids. As expected from the composition of the neonatal islet preparation, exocrine ductal elements comprised the major portion of these islet thrombi. Most islet cells contained insulin, (Figure 2) whereas lesser numbers contained glucagon in a more circumferential distribution (Figure 3). PP — immunoreactive cells and somatostatin positivity were seen sporadically.

Early on, the pancreatic thrombi underwent organization by inflammatory cells and attached to vascular endothelium. Subsequently, the pancreatic clumps appeared within the vascular wall and ultimately, by four weeks post transplant, individual islet cells had migrated away from the vessel through the limiting plate of the hepatic lobule to relocate immediately adjacent to hepatocytes. (Figure 4) This phenomenon was well demonstrated by the immunoperoxidase stain which showed insulin, glucagon, somatostatin, and PP cells able to migrate in this fashion.

The initial embolization of pancreatic fragments was associated with multiple microinfarcts of the hepatic parenchyma. However, within one week these infarcted areas were filled with regenerating hepatocytes and by four weeks post transplant they could not be distinguished from the surrounding liver tissue.

#### *Morphologic Appearance after One Year Post Transplant*

After 65 weeks, many large complex islet structures representing the organization of the larger thrombi were identified. Very few islet cell types were seen singly but almost always associated with these larger

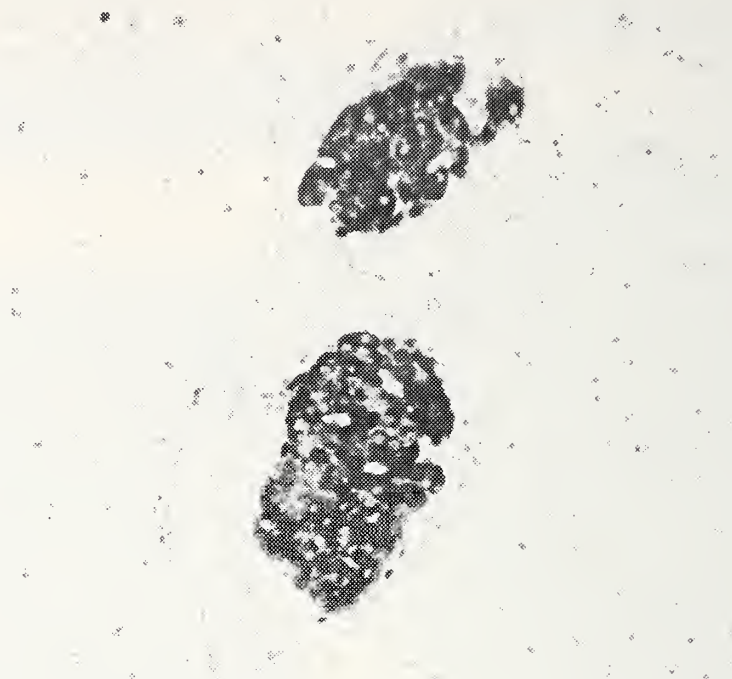


Fig. 2 — Islet thrombus showing two foci of strong insulin immunoreactivity at 24 hours post transplant. Associated exocrine tissue is still easily recognized at this stage. Immunoperoxidase. x 100.



Fig. 3 — Large islet with peripherally arranged glucagon-containing cells at 24 hours post transplant. Immunoperoxidase. x 100.



Fig. 4 — By one week post transplant, islet cells have migrated out of the vascular space and appear immediately adjacent to hepatocytes. Insulin. Immunoperoxidase. x 100.



structures. The majority of cells stained positively for insulin; however, substantial numbers of glucagon-, somatostatin-, and PP- immunoreactive cells were also present. The islet morphology recapitulated the normal adult rat pancreatic islet in many cases, with a central beta cell core staining positively for insulin, whereas glucagon, somatostatin, and PP cells assumed a peripheral location. A few islets had a different morphologic appearance, with strands of islet cells coursing out between the cords of hepatocytes in all directions and contiguous with them (Figure 5). Acinar tissue was, in general, greatly diminished; however, in one section showing a relatively large islet thrombus, acinar tissue with glandular differentiation could still be identified 65 weeks post transplant.

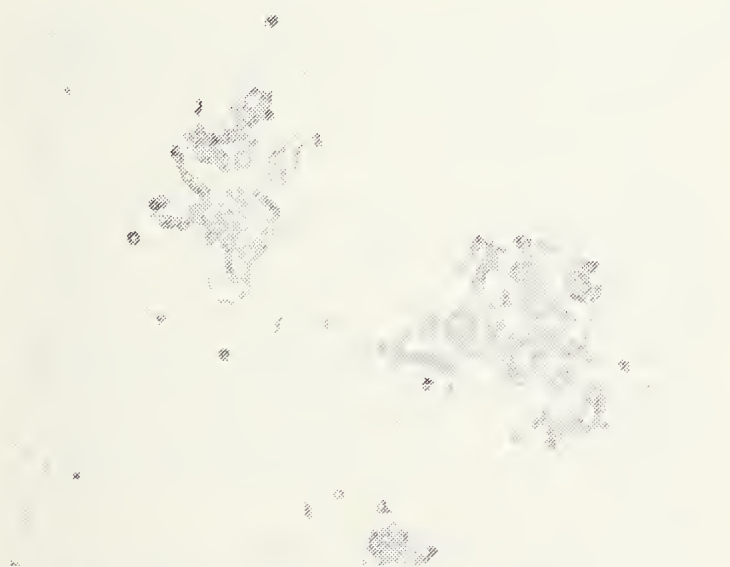


Fig. 5 — Complex arrangement of insulin-containing cells seen at 65 week post transplant. Recognizable exocrine elements are rare at this stage. Immunoperoxidase.  $\times 100$ .

### Discussion

The major goal of diabetes therapy today is to prevent the renal, ocular, and vascular complications. A prevailing hypothesis today maintains that lesions result from a lack of metabolic homeostasis, and that these complications will not develop if metabolic imbalances can be corrected. Recent studies in the laboratory animal support this contention.<sup>17,18</sup> Long term reversal of streptozotocin induced diabetes in the rat has been accomplished using neonatal islet preparations embolized to the liver via the portal vein.

Diabetic recipients of intraportally transplanted islets rapidly become normoglycemic after injecting islet preparation (one to nine days in this study). Histological examination of the recipient livers demonstrates islets which vary in size and are distributed throughout the liver according to the size of the embolized fragment. Although this embolization results in multiple microinfarcts, these are rapidly

restored and by four weeks cannot be recognized morphologically. Endothelialization of the pancreatic thrombi occurs within 48 hours, with incorporation into the vascular wall or periphery of the hepatic lobule by four weeks post transplant. The speed of this process also appears to be a function of the size of the initial embolized fragment.

Immunocytochemistry has been extremely useful in the localization of specific islet hormones within grafts recovered from various transplant sites. Hegre et al.<sup>19</sup> demonstrated insulin, glucagon, and somatostatin in islets transplanted into the peritoneal cavity of alloxan-induced diabetic rats. Using the unlabeled antibody enzyme technique, we have documented the survival and continued function of insulin-, glucagon-, somatostatin-, and PP- containing cells up to 65 weeks post transplant in cured diabetic rats. Erlandsen et al.<sup>20</sup> have described three zones within the normal adult rat islet. A central core of insulin-containing beta cells is surrounded by a zone of peripherally located glucagon cells, with somatostatin and PP cells occupying an intermediate position. This relationship among cell types is largely preserved even after enzyme digestion and intraportal transplantation as long as 65 weeks post transplant. The marked absence of single islet cells unassociated with larger islet structures at 65 weeks suggests that transplanted islet tissue has the capacity to continue growth and differentiation after transplantation. Hegre et al.<sup>19</sup> have observed mitotic figures within transplanted islet cells and Lazarow et al.<sup>21</sup> have quantitated morphological changes in fetal islet mass at the transplantation site. Therefore, even if the initial mass of islet tissue may not be enough to reverse the diabetic state, continued growth may result in a cure later on.

There is growing evidence that the morphological integrity of the pancreatic islet substructure is important in the complex interplay of regulatory influences that islet hormones exert on each other.<sup>22</sup> Although further clarification of the relationship between hormone secretion and islet microcirculation is needed, preserving islet structure seems to be an important factor for the ability of the islet graft to effectively correct the metabolic imbalance of diabetes. Our findings of long term survival of all known islet cell types in the rat further support the theory that homeostatic control of carbohydrate metabolism may be achieved through islet transplantation and raise the prospects for applying this technique to humans. Unfortunately, initial attempts to apply this technique clinically have been largely unsuccessful. First, the human pancreas differs from that of the rat in that it is a



less distensible and fibrous structure which does not lend itself to processing by conventional techniques. As a result, adequate yields of separated intact islets have been difficult to obtain. A second major obstacle is the immunogenicity of islets which has led to rapid rejection of transplanted grafts across strong histocompatibility barriers. Graft survival has been prolonged by immunosuppression or with the use of artificial chambers.<sup>23</sup> These "hybrid" devices employ a selectively permeable membrane to prevent contact of the islet cells with lymphocytes and antibodies but allow passage of glucose, insulin, and nutrients.

Najarian et al.<sup>24</sup> have performed islet tissue grafts in

seven immunosuppressed patients who had previously received kidney transplants for end stage diabetic nephropathy. Although normoglycemia was not achieved, insulin requirements were decreased transiently, and in one patient this reduction lasted for 17 months. Nevertheless, continued improvements in techniques for the isolation and preservation of islets<sup>25</sup> and efforts aimed at modification of graft immunogenicity by tissue culture<sup>26</sup> are encouraging and bring us ever closer to the possibility of future "islet banks". Clearly, however, the transition from the laboratory to the patient will be a major challenge.

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18-26. May be secured from the authors.

#### Cover Sculpture "Flight Instructor"

The cover sculpture by Dr. Don L. Carlon of Moorhead is of cast bronze, 21 inches in height. Dr. Carlon has been a metal sculptor for about ten years. His work is presented locally by the Lesch Gallery in Butler Square, Minneapolis.

A radiologist at St. Ansgar Hospital in Moorhead, Dr. Carlon has had three previous sculptures, published on MINNESOTA MEDICINE Covers: March, 1972, May, 1975 and January, 1976.



# Minnesota Department of Health

## Rabies: Epidemiology and Prophylaxis

January 10, 1978

ALLAIN M. HANKEY, M.S.\*† and JOHN S. ANDREWS, JR., M.D.\*†

**In 1978 Minnesota reported rabies in 196 animals of ten species. Many of these animals exposed humans to rabies. Physicians are frequently required to decide whether or not to treat exposed persons with rabies prophylaxis. Factors that should be considered include the epidemiology of rabies in Minnesota, the species of animal involved, the type of exposure, the exposure situation, and the effectiveness and risk of post-exposure prophylaxis. Brain specimens from possibly rabid animals need to be prepared and shipped correctly so that reliable results can be obtained from the laboratory.**

**Recommendations for postexposure prophylaxis include the use of rabies immune globulin in addition to duck embryo rabies vaccine. Duck embryo rabies vaccine should be used alone in persons who have had an adequate antibody level in the past two years.**

**E**ACH YEAR OVER one million people in the United States are bitten by animals. Practicing physicians are commonly confronted with the question of whether a person has been exposed to rabies virus and whether postexposure prophylaxis should be administered. Although rabies in humans is rare in the United States, an estimated 30,000 persons receive postexposure prophylaxis each year<sup>1</sup>.

### The Disease

Rabies is an acute viral disease caused by a virus belonging to the rhabdovirus group. In man the incubation period varies from 10 days to one year (usually 20-40 days), depending on a number of factors including the severity and site of the bite or laceration. It is short in wounds of the neck and head and longer in wounds of the extremities. The disease begins with nonspecific symptoms, often including apprehension, headache, fever, sore throat and irritability. Sensory changes, such as pain, tingling and paresthesias at the site of the inoculation, usually occur. Eventually, paralysis of the muscles of swallowing occurs, causing spasms during attempts to eat or drink. The disease is almost always fatal; however, three humans have recovered.

In domestic animals including dogs and cats, the incubation period varies from two weeks to over six

months (usually three weeks). Death occurs within three to seven days after the onset of clinical illness. Although the signs of rabies vary, two clinical syndromes have been described. In "furious" rabies animals are tense and hypersensitive to sounds and movements. In some cases they will attack inanimate objects, will have incoordinated gait, exaggerated movements and sexual excitement, and will produce frequent, loud, hoarse-sounding bellows or howls. The severe signs may be evident for 24-48 hours before the animals collapse in a paralyzed state and then die within a few hours. In "dumb" rabies early signs may include knuckling of the hind fetlocks, sagging and swaying of the hind quarters while walking, deviation of the tail to one side, decreased sensation, and drooling. These signs are followed by paralysis and death<sup>5</sup>.

The clinical course of rabies in wild animals is thought to be similar to that of domestic animals. However, the duration of clinical illness until death has not been well documented in many species.

### Pathophysiology

Rabies virus must come in contact with nerve tissue for man or animals to be at risk of acquiring rabies. Once in contact with nerve tissue, the virus travels along the peripheral nerves centrally to the spine and brain, where it replicates almost exclusively within the gray matter. The virus then passes centrifugally to the peripheral nerves and to other tissues, such as the salivary glands, adrenal medulla, kidney and heart<sup>2</sup>.

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Humans and animals inoculated with the virus on their heads and necks are at a greater risk of contracting rabies because of the relatively richer supply of peripheral nerves in this area than in the trunk<sup>3,4</sup>.

### Method of Transmission

Nearly all exposures resulting in human rabies are from animal bites that break the skin, although on occasion non-bite exposures from salival contamination of scratches or abrasions have caused disease<sup>9</sup>. Aerosol transmission of the virus has been documented, but only in the unique ecological conditions of the bat caves of Texas or in laboratory situations<sup>2,9-11</sup>. Rabies in humans has never been documented as the result of a bite from rodents or lagomorphs<sup>10</sup>.

### Prevalence

Rabies in humans in the U.S. has decreased from an average of 22 cases a year in 1946-1950 to only one to three cases a year since 1960<sup>6,7</sup>.

The number of cases of rabies in domestic animals in the U.S. has decreased similarly (Table 1). Wildlife rabies accounted for 86% of all confirmed rabies cases reported nationally in 1978. Reported cases of rabies in other wild animals, including raccoons, coyotes and bobcats, have increased primarily due to the establishment and spread of enzootic raccoon rabies in the southeastern states.

TABLE 1

Rabies in Animals, United States and Minnesota.  
1953 and 1978

	U.S. 1953	U.S. 1978	Minn. 1953	Minn. 1978
Dogs	5688	117	15	8
Cats	538	90	19	8
Other Domestic Animals	1118	250	31	42
Skunks	319	1698	50	33
Bats	8	548	0	3
Foxes	1033	147	2	1
Other Wild Animals	119	430	5	1
Total	8837	3280	122	196

### Epidemiology

Rabies exists in two ecologically distinct forms: urban rabies, propagated worldwide primarily by unimmunized domestic dogs, and sylvatic (rural) rabies, propagated by skunks, foxes, raccoons and insectivorous bats<sup>3,7</sup>.

In the U.S. and Canada, the urban form of rabies was most prevalent until the early 1950s<sup>3,6</sup>. Although the dog population increased through the early 1960s, mass vaccination of domestic animals and the destruction of stray animals have drastically reduced urban rabies<sup>8</sup>. Today, domestic animals, including

dogs and cats, usually contract rabies as the result of a bite from a rabid wild animal<sup>3</sup>. Rabies in other domestic animals is seen most frequently in cattle, although it does occur in swine, horses, sheep and goats.

Sylvatic rabies is propagated usually by bites within the species, but occasionally infected species transmit the disease to other wild animals. Sylvatic rabies in bats is reported in every state except Hawaii, which is rabies free. Rabies in skunks is most prevalent in the Midwest and Southwest. Rabies in foxes is most frequent in the Appalachians from New England to the South Atlantic states. The disease in raccoons is restricted primarily to Florida and Georgia<sup>3</sup>. Rabies is not endemic in wild rodents (rats, mice, squirrels, gophers, voles, etc.), lagomorphs (rabbits, hares and pikas), or domestic rodents (gerbils, guinea pigs, hamsters, etc.)<sup>9</sup>. Two flying squirrels comprised the only naturally occurring rodent rabies confirmed by CDC from 1960 through 1979.<sup>12</sup>

### Criteria for Testing Animals

If a person has been exposed to a dog or cat which is alive and available, it should be confined by a responsible individual and closely observed through day 10 after the exposure. If the dog or cat exhibits any abnormal signs during this period, it should be evaluated as soon as possible by a veterinarian. If the veterinarian suspects rabies, the dog or cat should be sacrificed and sent to the Minnesota Department of Health (MDH) for fluorescent antibody (FA) testing of its brain by the Division of Medical Laboratories. If the animal is a stray or unwanted animal, it should be confined for ten days before being sacrificed. If the animal is already dead, it should be sent to the MDH for FA testing.

If a domestic animal other than a dog or cat (cow, horse, etc.) exposes a human, a veterinarian should be consulted. If the veterinarian suspects rabies, the animal should be sacrificed and sent to MDH for FA testing.

If a person has been exposed to a wild animal of a species known to carry rabies, the animal should be immediately sacrificed without damaging its head. A dead wild animal which has bitten someone should be shipped immediately to MDH for FA testing of the animal's brain for the presence of rabies virus.

If a person has been bitten by a rodent or lagomorph, no test is needed.

### Preparation and Shipment of Specimens

Proper preparation of specimens is essential. The person handling the carcass of a possibly rabid animal



should use rubber or leather gloves. Immediately upon the death of the animal the head should be cut off close to the shoulders, leaving the cervical vertebrae and spinal cord attached. (If the animal is small, the entire animal can be sent to MDH.) For a dog weighing more than 30 pounds, horse, cow or other large animal, the lower jaw should be unjointed and the soft tissues of the neck cut off. If this is done, better chilling of the brain can be maintained enroute. If the brain has been damaged, a portion of the vertebral column with the spinal cord inside should be sent to MDH with the damaged head.

The specimen should be wrapped in two strong plastic bags, one inside the other. It should be chilled immediately and kept cool, but not frozen, until it is packed for shipment. For shipment, the double-wrapped specimen should be repacked in a cardboard box or other suitable container. Sufficient paper shreds or newspaper should be packed around it to absorb fluids in case of leakage. Ice should be added to the container to keep the specimen cool during shipment. (Dry ice should not be used.)

*Where there has not been any human exposure,* animal specimens should be sent to the University of Minnesota for testing:

Division of Veterinary Diagnostic  
Laboratories  
College of Veterinary Medicine  
University of Minnesota  
St. Paul, MN 55101

*If there has been a human exposure* (as defined above), specimens should be sent to:

Division of Medical Laboratories  
Minnesota Department of Health  
717 Delaware Street SE  
Minneapolis, MN 55440

The package should also bear the following direction to the package transporting service:

RUSH      PERISHABLE      KEEP COOL

To express agent at destination: Advise consignees immediately by telephone (612) 296-5475 on receipt of this package. If not during WORKING Hours and no answer at this number, notify the University of Minnesota Campus Police at (612) 373-3550.

Immediately prior to sending a specimen, the shipping room at the Minnesota Department of Health should be called (612-296-5475) with information on how and by which carrier the specimen is being sent and time of arrival in Minneapolis.

The following information regarding the biting animal and person bitten should be forwarded to the MDH with the specimen:

1. Name, address and telephone number of the owner of the animal
2. Account of illness or strange behavior of the animal
3. Dates of onset of symptoms and death of the animal
3. Method by which the animal was killed
5. Names, addresses and telephone numbers of people bitten or otherwise exposed
6. Names, addresses and telephone numbers of owners of other animals bitten or otherwise exposed
7. Physician(s) of person(s) bitten or otherwise exposed
8. Any pertinent information, such as whether or not the submitted animal is known to have been recently exposed to a possibly rabid animal

The Epidemiology Unit of the Minnesota Department of Health is available for consultation (612-296-5414) during the day and at night.

### Prevention

In Minnesota, three principles are involved in preventing rabies in humans: (1) prevent human exposure to rabid animals by urging people to avoid all wild animals, stray domestic animals and strangely behaving domestic animals, and through an effective community rabies control program. (dog or cat bites following provocation should not be considered exposure) (2) provide veterinarians, animal handlers and other high-risk persons with preexposure prophylaxis, and (3) provide postexposure prophylaxis.

#### Preexposure Prophylaxis

Veterinarians, trappers, animal handlers, certain laboratory workers and others with high occupational risk of exposure to rabies virus should receive an initial series of duck embryo antirabies vaccine (DEV) and boosters at regular intervals.

There are two recommended regimens for preexposure prophylaxis: (1) two 1 milliliter (ml) subcutaneous injections in the deltoid area one month apart, followed by a booster dose six months after the second injection; (2) three 1 ml subcutaneous injections at one-week intervals and a booster dose three months later. The first method is preferable and elicits a protective rabies antibody response in 80-90% of vaccinees. The second method is used when a rapid immunization is needed and results in a protective antibody response in 80% of vaccinees<sup>10</sup>.

Three additional points are important: (1) Recipients



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of preexposure prophylaxis should submit sera for rabies antibody testing two to four weeks after the initial series of injections (before the booster dose).<sup>\*</sup> A titer of 1:16 or greater is considered protective. Those individuals with antibody levels less than 1:16 should receive a second booster injection, followed two to four weeks later by repeat testing for antibody titer. Those with persistently inadequate titers should receive additional boosters and have additional serum specimens obtained until adequate antibody levels of 1:16 or greater are achieved. (2) All those who receive preexposure prophylaxis should receive booster injections every two years regardless of previous antibody titers. After these booster injections, antibody titers should be measured. (3) Individuals who receive preexposure prophylaxis must receive an abbreviated course of postexposure prophylaxis if exposed to a rabid animal.

### Postexposure Treatment

Since rabies can be contracted by humans only if the rabies virus penetrates the skin or gains access to the mucous membranes, an individual must have one of the following contacts with a rabid animal or possibly rabid animal to be considered at risk of contracting rabies: a bite that penetrates the skin or saliva contamination of an open cut, or abraded area of skin or mucous membrane.

Immediately after an exposure, wash and flush the wound (or exposed area) with soap and water, detergent or water alone. Cleaning the wound may be the most effective protective measure to prevent rabies and local infections. Then apply either 40-70% alcohol

TABLE 2

Reactions to Postexposure Prophylaxis  
With DEV in 116 Persons

Reactions	Number of Percent of	
	Reactions	Total
Immediate pain, stinging or burning at site of injection	116	100
Local erythema	54	47
Malaise	39	34
Local tenderness or lasting pain	38	33
Myalgia	31	27
Local induration	28	24
Regional adenopathy	21	18
Local pruritis	15	13
Temperature of 37.8°C (100°F) or more	15	13
Chills	6	5
Generalized adenopathy	3	3
Anaphylaxis	1	0.9

Rubin RH, Hattwick M. Adverse reactions to duck embryo rabies vaccine. *Ann Intern Med* 78:643-649, 1973 by permission.

or tincture or aqueous solution of iodine. Individuals who have had a primary series of tetanus immunizations should receive boosters if they have not been immunized within the past five years. Those who have never had a complete primary series of tetanus toxoid should begin this series. Antibiotics may be useful to prevent bacterial infection in bites.

The Figure may be used as a guide to determine if rabies immunizing products should be used.

Postexposure prophylaxis for individuals who have received preexposure prophylaxis and have had an adequate antibody level within the past two years, consists of five daily injections of DEV and a booster 20 days later. Passive immunization (RIG) should not be given as it may inhibit a rapid anamnestic response. A serum specimen should be obtained for rabies

<sup>\*</sup>These sera can be sent to the Minnesota Department of Health for forwarding to the Center for Disease Control. There is no charge for testing.

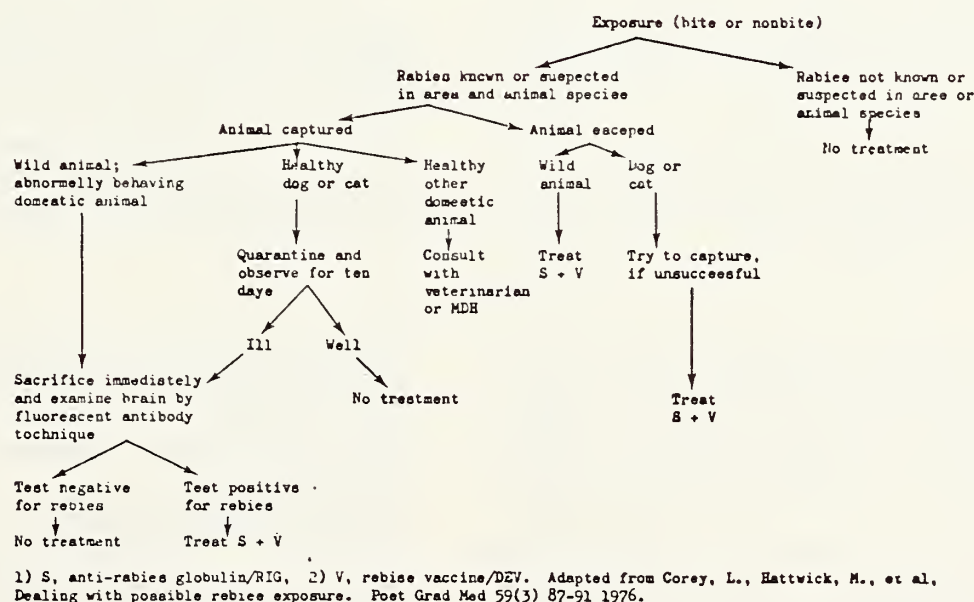


Figure — Algorithm of Postexposure Prophylaxis



antibody testing prior to administering the booster dose.

Postexposure prophylaxis for persons not known to have adequate antibodies to rabies should begin with rabies immune globulin (RIG). The dosage is 20 IU/kilogram of body weight (150 IU per ml). Half the dose should be infiltrated into the wound and half given intramuscularly. A 23-dose series of subcutaneous duck embryo rabies vaccine should begin as follows: one dose a day for 21 days (through day 21), one booster dose 10 days later (day 31) and one booster dose 10 days later (day 41). A serum specimen should be obtained prior to the booster dose on day 41 to determine antibody levels as described in *Preexposure Prophylaxis*.

*Rabies Immunizing Products*

Duck embryo vaccine (DEV) is a killed vaccine prepared from embryonated duck eggs infected with a fixed virus and inactivated with beta-propiolactone. It is supplied in 1 ml single-dose vials of freeze-dried vaccine with diluent ampoule and is recommended for active immunization against rabies<sup>10</sup>.

Approximately 424,000 persons received DEV between 1958 and 1971, and the following serious reactions were voluntarily reported: 22 cases of anaphylaxis, 11 of abdominal pain associated with nausea and vomiting, five of cranial or peripheral neuropathy, four of transverse myelitis, two of nonfatal encephalopathy, two of fatal encephalitis and one of thrombocytopenic purpura<sup>13</sup>. The two reported deaths occurred in individuals who may have actually died as a result of rabies. To determine the true incidence of reactions to the vaccine, prospective studies were carried out: 116 persons receiving postexposure therapy reported reactions as summarized in Table 2. Although DEV is associated with a high incidence of minor reactions, it rarely causes serious difficulty and can be safely used in rabies

\*The use of brand names is for identification of biologicals only and does not constitute endorsement by the PHS, U.S. Dept. HEW or the Minnesota Department of Health.

Minnesota Distributors of Rabies Immunizing Products

Brown Drug 1414 M. Avenue Sioux Falls, SD 57101 (605) 336-3150 stocks DEV and RIG	Northern Drug Co. 420 Commerce Street Duluth, MN 55801 (218)722-4791 stocks DEV only
Jewitt Drug 217 Railroad Avenue Aberdeen, SD 56401 (605) 225-0870 Stocks DEV only	Northwestern Drug Co. 2001 NE Kennedy Minneapolis, MN 55413 (612) 331-6550 stocks DEV and RIG
Mankato Brown Drug 153 Chestnut Mankato, MN 56001 (507) 345-5073 stocks DEV and RIG	Spence McCord Drug Co. 1502 Miller Drive LaCrosse, WI 54601 (608) 782-0885 stocks DEV and RIG
McKesson & Robbins Drug Co. 3230 Spruce Street Little Canada, MN 55110 (612) 482-5200 stocks DEV and RIG	Twin City Drug 900 North 3rd Street Minneapolis, MN 55401 (612) 339-7401 stocks DEV and RIG
McKesson & Robbins Drug Co. 720 Fourth Street North Fargo, ND 58102 (701) 235-3111 stocks DEV only	Yahr-Lange Drug, Inc. 200 Main LaCrosse, WI 54601 (608) 785-1200 stocks DEV only

prophylaxis.

Rabies immune globulin (RIG), produced by Cutter Laboratories, is marketed as Hyperab\*. This form of passive immunization is recommended in a regimen with vaccine. It replaces hyperimmune horse serum (or antirabies serum ARS), which was associated with a high incidence of serum sickness. RIG is produced by cold ethanol fractionation of plasma from hyperimmunized human donors. Neutralizing antibody content is standardized to contain 150 IU per ml. It is supplied in 2 ml (300 IU) and 10 ml (1,500 IU) vials for pediatric or adult use. Local pain and slight febrile response may follow injection of RIG<sup>10</sup>.

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# Minnesota Medical Association

## Writing of Prescriptions through Delegation

DONALD C. BELL, M.D.\*

"We has met the enemy and they is us." Pogo's paraphrasing of Admiral Perry's famous claim of naval victory can have no more fitting application than the situation that currently exists with certain physicians who inappropriately, if not illegally, delegate their prescription writing authority to non-physicians.

Abuses such as presigning prescription pads and delegated forging of prescriptions by physician extenders more than any other factor or combination of factors will encourage physician assistants and/or nurse practitioners to seek statutory authority to prescribe independently of physician supervision.

Most often these practices are permitted in settings where physician extenders such as physician's assistants and nurse practitioners see patients through the general supervision of the physician but where the physician does not have direct contact with the patient. The physicians rationalize that the practicalities of these situations dictate the necessity for delegation of prescriptive authority. Prescribing by non-physicians is known to occur in family planning clinics, rural settings staffed by physician assistants or nurse practitioners and in certain HMOs who under intense pressure to hold down costs utilize physician extenders in large numbers.

Minnesota law does not permit pharmacists to knowingly fill prescriptions signed only by nurse practitioners or physician's assistants. A pharmacist who honors such a prescription is breaking the law. Moreover, should the prescription produce an untoward effect and litigation ensues the physician who authorized the prescribing may expose him or herself to unnecessary legal liability and perhaps a defenseless case. While presigning the prescription pad may make the act of delegated prescribing authority technically legal, it is poor medical practice even where strict protocols exist.

Pharmacists are especially ill at ease, and understandably so, when presented with a prescription they suspect or know to be signed only by a non-physician. Should they refuse to fill the prescription they risk the good will of the customer and perhaps the physician who must be called to confirm the order. To fill the prescription without questioning, places the pharmacist in ethical or legal jeopardy.

To solve this dilemma, why not simply change the law to conform to these current practices? Simply because it would not be in the public's best interest to permit non-physicians to make independent medical judgments and decisions regarding patient's prescription requirements. It would mean that the public would lose its protection from unqualified persons dispensing medical care.

It may be helpful to elaborate further on this subject by considering the nurse practitioners as a case in point. The term, "nurse practitioner" itself has no legal definition in Minnesota at this time. The nursing profession has its own definition based on certain training requirements and will undoubtedly seek credentialing in the future. At the present time, however, any nurse can legally define her or himself as a nurse practitioner, and no authoritative body can currently dispute the title.

When discussing the question of prescription writing authority, some nurse practitioners imply that they do not envision themselves as functioning other than in a collaborative role with a physician. However, when pressed by direct question many nurse practitioners admit that they would like to have "independent" prescription writing authority. Indeed, it would be difficult to design legislation that would give nurse practitioners the authority to prescribe but limit the setting under which they could do so. What would likely result is the establishment of independent practices by nurse practitioners practicing limited medicine and functioning as primary care providers, thus further fragmenting the medical care delivery system.

Since certain elements in nursing are encouraging this, it would be wise for the public to consider the qualifications of nurse practitioners as opposed to physicians. A typical baccalaureate nursing curriculum includes: two semesters of bi-weekly two-hour lectures on medical and surgical nursing and two months of study of pharmacology as part of the four-year program. Added to this is the one-year post graduate training in clinical skills in the nurse practitioner program itself. By contrast, a physician receives a minimum of five years of post-college training, and in most cases it is from six to nine years. In addition to this there are many hours per year of continuing education which physicians engage in. The result is

\*Representative of the MMA on a Discussion Group comprised of representatives of pharmacy, nursing and medicine studying, dispensing, and prescribing issues.



that society has reasonable assurance that medical treatment is performed with the knowledge, skill and, perspective such training affords.

Should the Legislature decide that nurse practitioners or any health occupational group with minimal training in medicine be allowed to prescribe the precedent will be set, and physician's assistants, midwives, clinical psychologists, optometrists, and, of course, chiropractors may seek to quickly acquire similar privileges — and why not?

It thus should behoove the Minnesota Medical Association to take a strong stand on this issue. All argumentation in favor of the current abuses of the physician's prescriptive authority should be examined in comparison to the inevitable results of legalizing these practices. We need to decide if we want to maintain the privilege of limitation on prescribing or not, and if we do, we need to make our practices conform to the current law. We can't have our cake and eat it too!

### Book Review

#### **The Heritage of Aviation Medicine: An Annotated Directory of Early Artifacts**

By Robert J. Benford. 121 pp., illustrated. Washington, D.C.: Aerospace Medical Association, 1979.

This paperback volume is a listing of items of equipment used in aviation medicine or for aircrew protection from approximately 1910 to 1955.

Categories included are Goggles and Helmets, Flying Clothing, Protective Garments, including pressure suits, armor and G-suits, Oxygen Masks and Regulators, Flight Medicine Equipment and Survival and Rescue Gear. There is a bibliography of 5 pages. Each item is described, and a code number given which determines where the item can be found. Many of the items are illustrated in black-and-white photos of rather fuzzy quality.

I do not think this book will interest a great many people. Its chief value would be to persons doing research in the history of aviation medicine who could use this book to locate particular items. Equipment from several countries is shown, including the United States, Britain, Canada, France, Germany and Japan. It is instructive to see such devices as oxygen masks and regulators progress from primitive to sophisticated levels.

Certain comments are possibly naive. A dog-hide immersion suit is shown. The text states that Hurricane pilots wore it for convoy protection duty. Those planes were launched via catapults from freighters on the North Atlantic in 1942-1943. Since there were not sufficient aircraft carriers available to protect the convoys, these RAF "Hurricat" pilots were sent to attack Luftwaffe patrol aircraft. The Hurricanes normally lacked sufficient fuel to reach land. Many comments have been made about the strange Japanese who accepted suicidal Kamikaze missions. The text says "with fuel nearly exhausted, the pilot then ditched ahead of the convoy and was picked up".

What the author fails to say is that the water temperature was around freezing and practically all of the pilots who managed to exit from their ditched craft drowned. These pilots from places like Kenora and Winnipeg were sent on missions, born of desperation, very near to Kamikaze suicide.

The one-eyed Wiley Post is there, proudly modeling his pressure suit and holding a helmet that looks like a Jules Verne original, along with many of his colorful contemporaries who traveled along the fine line between courage and foolhardiness. For me, these photos alone were worth the price of admission.

Samuel Berman, M.D.  
AOPA #235589  
Minneapolis, Minnesota



# Address

## Reflections on Life's Odyssey for Medical School Graduates.

OWEN H. WANGENSTEEN, M.D.\*

THE MINNESOTA MEDICAL ALUMNI ASSOCIATION welcomes and salutes you today. Each of you has undoubtedly found your pace and stride, but for many of our school's more recent graduates your era of greatest accomplishment will not be reached for another 10 to 15 years. Of my class of 73 in 1921-22, of which seven were women, all were alive save two on our 25th anniversary; on our 40th, more than 40 percent were no longer amongst the living. Today, a mere handful survive in their early 80s. It would appear that the longevity of American physicians has continued on the increase since World War II days.<sup>1</sup> In business, the professions, and in universities mandated retirement is usually looked upon as a "frosting on the cake" for services well performed. Most of my classmates who went to spend their declining years in the land of the sun are gone. However alluring life in the sun may appear to be, it is difficult to believe it can be as attractive or satisfying as contented work. Moreover, the mind keeps sharper upon retirement, when still applied to tasks once found stimulating. The warning of the psalmist (90;10) "The years of our lives are three-score and ten; yet, if by strength they be four-score years, yet is their strength but labor and sorrow" is not entirely correct; to be certain, there are some handicaps, but they are far more acceptable than any currently available alternative.

The Russian emigré Eli Metchnikoff<sup>2</sup> (1845-1916), of the Pasteur Institute and author of the cellular theory of immunity (1885), wrote two monographs in which he dealt with old age and *The Nature of Man* (1906), in *The Prolongation of Life* (1907) in which he promulgated the thesis that bacteria of the alimentary tract were responsible for many diseases. He believed and proposed that changing the bacterial flora by daily ingestion of a yogurt-like milk, life could be extended to 140 years. He abstained completely from alcohol and tobacco, believing they were conducive to arteriosclerosis. Yet, he died at 71, spending the last two years of his life in daily agony from cardiac angina, relieved only by narcotics. Today, coronary artery by-pass surgery could very likely have provided

relief and hope for extended years. The centenarians amongst us, however, remain very few indeed.

The passions and wants of all of us are many. To be a good doctor is undoubtedly the chief objective of most young physicians, which puts a high demand upon Service, as does also the desire to achieve recognized success in the profession. Some of you are dedicating your lives to investigative studies and teaching, which can prove very rewarding and soul-satisfying. Where is my work taking me, some of you ask. Examine critically your work day, month in and year out, and the answer becomes quite apparent. If your daily work schedule is not in accord with your life's objectives, a drastic change may effect the needed transition, which becomes increasingly difficult to achieve after 40.

The spur of encouragement undoubtedly constitutes the very basis of successful preceptorship, perhaps nowhere better illustrated than Ralph Waldo Emerson's futile efforts to push an unwilling calf into the barn. The kitchen maid, noting the proceedings, came out, put a finger into the calf's mouth, which then went along eagerly. The teacher who discourages his or her students does a disservice to the educative process, a statement most of you can verify from your own personal experience.

The mind grows by what it feeds upon — associates, books, teachers, and an atmosphere encouraging to scholarly pursuits. Bernard Shaw's definition of a learned man as an idler who kills time at study is not far off the mark. Every serious student comes to know from experience how difficult the discovery of a new fact is; the cost in time, sleepless nights, and in unrelenting inquiry for months and years on end. The joy of discovery is undoubtedly one of life's most treasured satisfactions and can only be fully appreciated by those who have experienced it. If every investigator could taste of this Elysian delight in his first research adventure, undoubtedly many more would try their fate and fortune in the sphere of the unknown.

The only Hallmark of distinction among scientists is accomplishment, and when the love of learning and a yearning to be able to contribute to creative scholarship consumes the young student, he is lifted above a primary concern for material possessions. Once the

\*Regents' Professor Emeritus, Department of Surgery, University of Minnesota, Minneapolis, Minnesota.

Presented May 19, 1979 at meeting of representatives of the Medical School graduates from 1929-1969, in a symposial discussion on New Horizons in Minnesota Medicine.



# ANUSOL-HC<sup>®</sup>

SUPPOSITORIES/CREAM WITH HYDROCORTISONE ACETATE

#1 prescribed hemorrhoidal product

IT WAS  
NUMBER ONE  
IN 1959

AND IT STILL IS...

The professional source of  
modern anorectal comfort

## ANUSOL-HC<sup>®</sup> SUPPOSITORIES

Hemorrhoidal Suppositories

## ANUSOL-HC<sup>®</sup> CREAM

Rectal Cream with Hydrocortisone Acetate

**Caution:** Federal law prohibits dispensing without prescription.

**Description:** Each Anusol-HC Suppository contains hydrocortisone acetate, 10.0 mg; bismuth subgallate, 2.25%; bismuth resorcin compound, 1.75%; benzyl benzoate, 1.2%; Peruvian balsam, 1.8%; zinc oxide, 11.0%; also contains the following inactive ingredients: dibasic calcium phosphate, and certified coloring in a hydrogenated vegetable oil base.

Each gram of Anusol-HC Cream contains hydrocortisone acetate, 5.0 mg; bismuth subgallate, 22.5 mg; bismuth resorcin compound, 17.5 mg; benzyl benzoate, 12.0 mg; Peruvian balsam, 18.0 mg; zinc oxide, 110.0 mg; also contains the following inactive ingredients: propylene glycol, propylparaben, methylparaben, polysorbate 60 and sorbitan monostearate in a water-miscible base of mineral oil, glyceryl stearate and water.

**Indications:** Anusol-HC Suppositories and Anusol-HC Cream are adjunctive therapy for the symptomatic relief of pain and discomfort in: external and internal hemorrhoids, proctitis, papillitis, cryptitis, anal fissures, incomplete fistulas and relief of local pain and discomfort following anorectal surgery.

Anusol-HC Cream is also indicated for pruritus ani.

Anusol-HC is especially indicated when inflammation is present. After acute symptoms subside, most patients can be maintained on regular Anusol<sup>®</sup> Suppositories or Ointment.

**Contraindications:** Anusol-HC Suppositories and Anusol-HC Cream are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

**Warnings:** The safe use of topical steroids during pregnancy has not been fully established. Therefore, during pregnancy, they should not be used unnecessarily on extensive areas, in large amounts or for prolonged periods of time.

**Precautions:** Symptomatic relief should not delay definitive diagnoses or treatment.

If irritation develops, Anusol-HC Suppositories and Anusol-HC Cream should be discontinued and appropriate therapy instituted.

In the presence of an infection the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Care should be taken when using the corticosteroid hydrocortisone acetate in children and infants.

Anusol-HC is not for ophthalmic use.

**Dosage and Administration:** Anusol-HC Suppositories — Adults: Remove foil wrapper and insert suppository into the anus. Insert one suppository in the morning and one at

bedtime for 3 to 6 days or until inflammation subsides. Then maintain patient comfort with regular Anusol Suppositories.

**Anusol-HC Cream — Adults:** After gentle bathing and drying of the anal area, remove tube cap and apply to the exterior surface and gently rub in. For internal use, attach the plastic applicator and insert into the anus by applying gentle continuous pressure. Then squeeze the tube to deliver medication. Cream should be applied 3 or 4 times a day for 3 to 6 days until inflammation subsides. Then maintain patient comfort with regular Anusol Ointment.

**NOTE:** If staining from either of the above products occurs, the stain may be removed from fabric by hand or machine washing with household detergent.

**How Supplied:** Anusol-HC Suppositories — boxes of 12 (N 0047-0089-12) and boxes of 24 (N 0047-0089-24) in silver foil strips with Anusol-HC W/C printed in black.

Anusol-HC Cream — one-ounce tube (N 0047-0090-01) with plastic applicator.

Store between 59°-86° F (15°-30° C).

Full information is available on request.

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inspiration is fired, the young scholar has come to an important turning point in his or her career and is well along the Damascus road to an appreciation of the nobility of scholarly pursuits, an attitude of mind that deserves cultivation in all universities and their colleges, including medical schools.

### A Look Back

As you celebrate today the anniversary of your graduation from medical school, and the 91st anniversary of the medical school's history, let us look back briefly to its origins.<sup>3,4</sup> William Folwell, Cyrus Northrup, and George Edgar Vincent were successively our university's presidents in the early years. Perry Millard, Parks Ritchie, Frank Westbrook and Elias Potter Lyon were the medical school's Deans over that period of 48 years (1888-1936).

Under the Vincent-Lyon thrust, the school was propelled forward from a mediocre, self-satisfied, institution, projected into the orbit of medical schools of first rank. Vincent was determined to improve the quality of the school's staff. When Lyon came on the scene in the first week of September 1913, he realized he had become plunged into a veritable hornet's nest over Vincent's mandated resignations in the faculty, and the vitriolic issue of the University's affiliation at the graduate school level with the Mayo Clinic and Foundation. Lyon withstood the storm by patient, compassionate, sympathetic, and discerning attention to the basic issues. Shortly after Vincent's departure to assume the presidency of the Rockefeller Foundation in June 1917, Minnesota's legislature, listening attentively, and heeding a plea from Regent William J. Mayo, agreed to legalize and thus to initiate the affiliation.

Lyon's first years at our University, apart from the bitter controversy just related, concerned establishment of strong Heads in all the preclinical sciences. Our department of anatomy in that period, under C. M. Jackson, probably had the strongest faculty in the nation. The strategic appointments of E. T. Bell in pathology, Wilford Larson in microbiology, Arthur Hirschfelder in pharmacology, and Maurice Visscher in physiology lent great strength to the school's preclinical faculty.

In the twenties and up to superannuation in 1936, Lyon's primary concern was building a strong full-time clinical faculty. Some of his remarkable appointments of this period in time were Leonard Rowntree in medicine, J. Charnley McKinley in neurology, George Fahr in medicine, Irvine McQuarrie in pediatrics, Leo Rigler in radiology, and Cecil J.

Watson in medicine, all of whom became outstanding exponents of their disciplines. They were largely unproved young men, a circumstance involving some risks. But is it not the function of a successful educator to recognize unusual talent before it becomes known to all the world? Lyon undoubtedly knew of the unusual good fortune of William Henry Welch in utilizing the same device in establishing The Hopkins' first medical faculty in the last decade of the 19th century. In retrospect, it probably is appropriate to note that of all the superb appointments made to the staff of this University by Vincent during his brief six years (1911-1917) here, typified by Lotus Delta Coffman in education, Guy Stanton Ford as Dean of the graduate school, and Walter C. Coffey, Dean of agriculture, all of whom in time became presidents of our University, Vincent's appointment of Lyon to the Deanship of our medical school probably has come to have the greatest and most durable impact upon the future of our University's colleges. Lyon was the primary architect of the fortunes of the University's medical school, certainly one of the finest colleges in our University today, but yet like all the others susceptible of improvement.

Over the years, our medical school has been blessed with a large number of superb administrative officers who have greatly enlarged and accelerated its growth, including Harold S. Diehl, Robert B. Howard, Neal Gault, Lyle A. French, and several others. Moreover, the largesse of the American people through its Congress since World War II days also has added considerably. The complexity of medical education and costs have increased considerably in recent years, but our school continues strong in virtually all its teaching disciplines.

E. E. Slosson<sup>5</sup> of Cornell (1910), in writing of great American universities, said that a Doctor of Divinity, President of Harvard and predecessor of C. W. Eliot, ended every chapel service with the prayer, "God bless Harvard and all inferior institutions." That prayer obviously has been abundantly answered throughout the breadth of our great land. Medical schools of the first rank today dot its geography. Harvard University was founded by our Pilgrim fathers in 1636, only 16 years after the first colonists settled at Plymouth Rock in 1620. Yet, Richard Shryock,<sup>6</sup> late great medical historian, wrote (1953) that the first true American university was The Johns Hopkins founded in 1876, 240 years after Harvard came into being. Harvard, said Shryock, was concerned primarily in the dispersion and dissemination of knowledge. The



mission and special concern of The Hopkins' medical faculty, on the contrary, was with medicine's advance and progress, undoubtedly a more accurate assessment of the precise nature of a true university, as distinguished from a college.

The finest possession of all universities is the power to appoint and select its faculties. One needs only to reflect upon what Daniel Coit Gilman, John Shaw Billings, and William Henry Welch did for The Hopkins in their respective roles as president, counselor and dean. During his 23 years at Minnesota (1913-36), Lyon may truly be said to have been the counterpart of Welch of an earlier day.

Twenty years ago in the 1959 sessions of the American College of Surgeons, it was the speaker's privilege to introduce the new president, that he was born in this century, evoked such spontaneous and prolonged applause that only after a delay of several minutes was it possible to announce his name, Robert M. Zollinger, one of the great American surgeons of this generation.

What of the Future? Since World War II days, the entire world has witnessed the tremendously increased confidence in research that its peoples have come to accept and appreciate for the promotion of human welfare. Many individuals in our medical school staff today have available for their research many times the commitment to the entire medical school faculty in the 1930s, indeed years of impressive frugality. When one reflects on the changes that have come about through virtual elimination of tuberculosis in Western countries; that poliomyelitis, empyema, bronchiectasis and infectious fevers too have almost disappeared through specific therapy, one comes to realize what 20th-century research has meant for medical progress and human welfare. So, too, insulin, cortisone, sulphanilamide, penicillin, streptomycin, including other antibiotics, and vitamin B 12, have altered significantly the medical scene for the better for both patients and physicians the world over. The past 50 years of this century through research have placed in the hands of physicians a veritable host of specific remedies that have enlarged and increased the therapeutic reach and accomplishments of physicians everywhere. Moreover, we can be certain that the last two decades of the 20th century will witness many medical advances through research not yet available. Surgery's most important contribution to medicine's progress in the last three decades has been intracardiac surgery. When the rejection phenomenon of homotransplantation of organs and of skin is completely overcome, surgery will have contributed very significantly

additionally to medicine's progress. The present achievement with kidney, heart and liver transplants provides considerable encouragement for the future.

### **How Minnesota Acquired its First Full-Time Surgical Chairman.**

Dean Lyon was anxious to establish a full-time appointee to chair the department of surgery. Harvey Cushing sent Francis Newton from Harvard to scrutinize the situation in Minnesota in 1925. Newton surveyed the opportunity and remarked, "There is nothing here and there never will be." Mont Reid of The Hopkins came via Cincinnati in early 1927 and concluded, as had Newton, that the University of Minnesota's medical school offered no bright prospects. Neither Newton nor Reid stayed long enough to sense the love of learning then emerging in the medical school faculty. Only a part of the story, however, has been told.

Sometime after Reid's visit here in 1927, Dr. Hilding Berglund, professor of medicine, provided a dinner at his home on a Sunday evening for a number of the medical faculty to try to persuade Dr. Arnold Schwyzer, Nestor of surgery in the Twin Cities, to take on the chairmanship of the department on a full-time basis. Support for this proposal among all assembled was very enthusiastic. The dessert course came along during this lively discussion, an attractive ice cream pie frozen over dry ice. As our host strove to cut into the solidly frozen pie, it slipped onto the floor; being the youngest guest present, your speaker felt it his duty to deliver it to the kitchen; asking the hostess, Helene Berglund, if she could provide two tall pitchers of steaming hot water and some long sharp kitchen knives. The faculty members present that evening apparently constituted the medical school's Search Committee. Schwyzer unfortunately declined their overtures. In the light of the many difficulties surrounding finding a suitable candidate for the professorship, the Search Committee probably concluded that a youngster who had the ingenuity to salvage the evening's final episode might do as their professor of surgery. So, with Dean Lyon's complete support, your speaker was sent abroad for somewhat more than a year with a monthly allowance of \$200, as a "sabbatical" from the University, to study the methods of great teachers of surgery in Switzerland, Vienna, Germany, and Britain. It was a wonderful experience. By late 1929, it became apparent that Dean Lyon's advice concerning the new chairman of the department had been fully agreed to by the faculty, on the recommendation of the Search Committee.



A few years later, in early May 1933, the appointee's competence to guide the destinies of the department was challenged by our new Dean of biological sciences, Richard Scammon, brilliant anatomist and the medical school's finest lecturer, and by this former protégé and appointee as hospital director, Halbert Dunn. Fortunately this brief skirmish with the new administrative officers of the School and Hospital was survived through loyal support of the prior part-time Professor of Surgery, Arthur C. Strachauer, and great friends within the medical faculty, Dean Lyon, President Lotus D. Coffman and Regent William J. Mayo. This timely experience sharpened considerably the appointee's motivation, persuading him to remain at Minnesota, despite offers from prestigious medical centers, to justify the confidence reposed in him when he had not yet won the full trust of all his associates.

### Rewards of Effective Teaching

Little has been said so far concerning the rewards of teaching, but since Plato of the 4th century B.C. taught in the Groves of Academe, it has frequently been said that the effective teacher, more than anyone else, is most likely to affect eternity through his intellectual progeny. Is it not the function of the teacher to strive to train pupils and protégés that will excel him in accomplishment?

A great boon to American medical education came in post-World War II days with reorganization of American Veterans Hospitals in metropolitan medical school areas under the supervision of Deans' Committees, an innovation we owe to a former Minnesotan, Paul Magnuson, who spent the major portion of his professional life in Chicago — certainly one of the truly great contributions to the American medical educative process of this century.

Your classes have been far better taught than mine of 1921-22; so too, the class of 1979 undoubtedly has enjoyed educational privileges unavailable in 1969. The democratic people of Minnesota value highly their institutions of higher learning and have liberally supported their University and its medical school, as has also our federal government through its National Institutes of Health. Two centuries ago when the penny had purchasing power, Samuel Johnson, author of the *Dictionary of the English Language* (1755), remarked, "One can live on 6£ sterling a year or any multiple thereof." There is a wide difference in latitude of choice between wants and needs, as each one of us comes to know. All loyal citizens of Minnesota, too,

through frugal living and generous public philanthropy, can help recreate for the State of Minnesota the Image which its Territorial Legislature (1849) conceived: "Minnesota, The Star of the North."<sup>7</sup> The high profile which those wise and far-seeing legislators envisaged for Minnesota 130 years ago, we can help to perpetuate.

Despite its long and arduous winters and high taxes, Minnesota continues to preserve an atmosphere friendly, warm and conducive to good living and to the acquisition and promotion of learning. Yes, we could wish for more, but those qualities of life which Minnesota strongly supports are among life's finest, lending its talented sons and daughters a wonderful opportunity for accomplishment and a rewarding and satisfying life.

In response to an inquiry, how after a year of marriage she found it, Sally my wife, replied: "Not half as bad as I thought it was going to be." That is about the way we have found retirement, too. In the presence of this distinguished company and good friends, your speaker would like to say how beholden he has been these many years to our University and its generous medical school administrative officers for unexcelled opportunities, and for the warm cooperation of wonderful associates.

When William Henry Welch, America's leading medical educator, turned 80, the New York Academy of Medicine tendered him a great dinner,<sup>8,9</sup> and when asked if granted a second chance in life, would he be willing to do it again, Welch replied in the negative, saying he had used up so much luck in this life, he could not possibly duplicate it. Though far from being a Prince Charming, only to whom in legend such privileges have been available, to a similar query, this surgeon would reply in the affirmative. Life in the academic arena has been extremely satisfying and rewarding. Acceptance of such a proposal, however, would be conditioned that in the reincarnation, my best friend and lovely wife Sally accompany me. Welch, it is to be recalled, was a lifelong bachelor. A happy and contented marriage does provide its partners perhaps the most fortunate and felicitous state of being in this life.

Finally, warm thanks are owing Dean Neal Gault, and his associates for the great privilege of addressing you on this happy occasion. May all of you in future years find in your chosen spheres of activity in the great Profession of Medicine, the satisfactions, rewards and happiness you continue to seek. Your paths too in future years will cross often with your Foster Mother, your Alma Mater, to whom all graduates of our Medical School are deeply beholden.

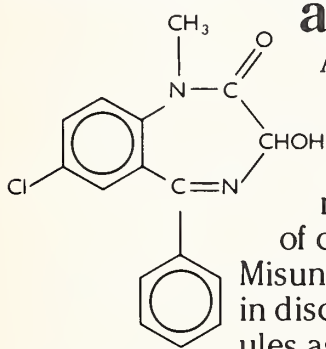
<sup>7</sup>References will be found on page 320.



## Aspects of Management

# What to tell your patients when you prescribe Valium® (diazepam/Roche)

### Survey shows significant correlation between comprehension and compliance



A study of compliance patterns reveals that more than 6 out of 10 patients made errors in self-administration of prescribed medication, largely due to lack of comprehension.\*

Misunderstanding of directions resulted in discrepancies in dosage schedules as well as in length of therapy.

Since evidence suggests that expanded verbal instructions may encourage compliance, the patient receiving Valium can benefit from your explanation of the dosage regimen, what response to expect from therapy and when to expect it.

### What Valium (diazepam/Roche) can do

Your patients should know that 1) you are prescribing Valium as an adjunct to an overall program for the treatment of anxiety, and 2) Valium is given to relieve the symptoms of excessive anxiety and psychic tension while you help the patient to explore and deal with the underlying cause of his psychic tension.

Patients often interpret manifestations of anxiety, such as palpitations, hyperventilation, fatigue and muscle tension, as symptoms of a serious disease. However, when they

learn that these symptoms can be relieved by Valium therapy, patients can more readily understand the psychosomatic origin of their symptoms and to accept the nonpharmacologic measures you may recommend.

The time you devote to these explanations can be a therapeutic measure in itself. Most anxious patients respond to and benefit from a frank discussion with an objective, sympathetic professional.

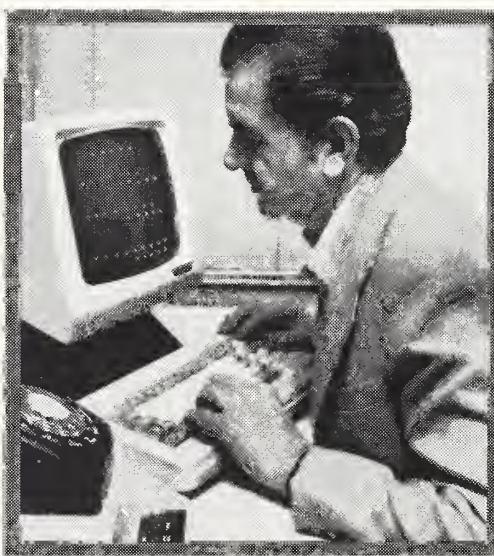
At the start of treatment, establishing therapeutic goals helps the patient to learn *what* to expect and *when* to expect it. Patients should also be informed that the medication will be gradually reduced and discontinued upon attainment of the therapeutic goal.

Tapering of dosage is rarely necessary in short-term therapy, but when consistently higher doses are used for extended periods, patients should know that the gradual reduction of medication will be implemented in order to avoid sudden recurrence of symptoms or possible withdrawal symptoms.

Such recurrence is unlikely when the causes of the anxiety have been worked out satisfactorily within your overall treatment program.

### What Valium (diazepam/Roche) can't do

It should be emphasized that there is no "magic" in any antianxiety tablet; that medication is not prescribed as a problem solver. Instead, Valium is being prescribed *as a temporary measure to relieve symptoms* generated by excessive anxiety and psychic tension.



\* Boyd JR, et al: *Am J Hosp Pharm* 31: 485-491, May 1974

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety associated with anxiety disorders, transient situational disturbances and functional or organic disorders; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms, or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy). The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders,

possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics,



## Practical pointers on taking antianxiety medications

**do's** Patients should be instructed to keep to their dosage schedule exactly as prescribed. If they miss a dose, they should not try to make it up by taking two doses the next time. Ask them to contact you promptly if they experience worrisome side effects.

Explain that drowsiness is a common reaction to almost all calming agents, but that it usually subsides in a few days. Urge the patient to contact you for a possible dosage adjustment if drowsiness or other reactions persist.

Just as you request a complete list of all medications the patient is taking, suggest that this list be given to any other physician treating her/him.

Like all medicines, Valium should be kept out of reach of children and young people. Old or unused medication should be discarded.

**and don'ts** Since drowsiness is an occasional problem, patients should be advised against driving or operating hazardous machinery until they see how the medication affects them. They should also know that tranquilizers increase the effects of alcoholic beverages, which should therefore be avoided. Also, warn patients against simultaneous use of drugs that depress the central nervous system, particularly sedative hypnotics.

Patients should be aware of the importance of not sharing their medications with friends and neighbors; they should know that what you have prescribed for them may be contraindicated for others.

# Valium<sup>®</sup> 2-mg, 5-mg, 10-mg scored tablets

## diazepam/Roche

An important adjunct to your treatment program for excessive psychic tension

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed, adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium<sup>®</sup> (diazepam/Roche) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available in trays of 10.



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barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



# History

## The Osler Medical Historical Society

Mayo Foundation "Chapter," August 28, 1920-July 3, 1925

RUTH J. MANN, B.S.\* and JACK D. KEY, M.A., M.S.†

The Osler Medical Historical Society was organized in Rochester, Minnesota, on August 28, 1920, in an attempt to perpetuate the ideals of Osler and to inspire the study of medical history. Under the leadership of the distinguished pathologist, Dr. William Carpenter MacCarty, the Society held meetings on a fairly regular monthly schedule until July 3, 1925, when the pressure of professional responsibilities prevented most of the members from participating in the Society's activities. Thus, through his student, W. C. MacCarty, Osler's influence in the humanistic study of medical history was felt during the early years of the Mayo Clinic. This tradition has continued at the Mayo Foundation in the fellowship and endeavor of the members of the *Mayo Foundation History of Medicine Society*. Today more than 300 Mayo physicians, scientists, and paramedical personnel participate in the activities of this successor to the Osler Medical Historical Society.

WILLIAM CARPENTER MACCARTY, 1880-1964 (Figure 1), was born in Louisville, Kentucky. He received his undergraduate training at the University of Kentucky. When he decided to study medicine, his chemistry teacher, Dr. Chase Palmer, convinced him he should attend the new medical school just opened under the deanship of a Dr. Welch.<sup>1</sup> So, MacCarty went to Johns Hopkins University, graduating in 1904 with the degree of Doctor of Medicine. While in Baltimore, he was not only a student of Welch, but also of Osler, Halsted, and Kelly, thus participating in and benefiting from one of the most important and interesting experiments in medical education anywhere at any time. After postgraduate study in Germany, he entered the Mayo Clinic as assistant pathologist in 1907 and became head of a section on surgical pathology in 1909. For the rest of his life, he was one of those who influenced another of the most exciting developments in medical practice and education, that is, the private coordinated group practice of medicine that evolved at the Mayo Clinic and Mayo Foundation.

He was the first person at the Mayo Clinic to use animals in experimental investigations. With Dr. L. B. Wilson he introduced the technique of immediate

microscopic examination of tissue removed during surgery and was a notable pioneer investigator in this field.<sup>2</sup>

When MacCarty was a student at Johns Hopkins he became convinced of the importance of the study of medical history. He belonged to the Johns Hopkins Medical Historical Society. When he became a staff member of the Mayo Clinic in 1907, he lectured on

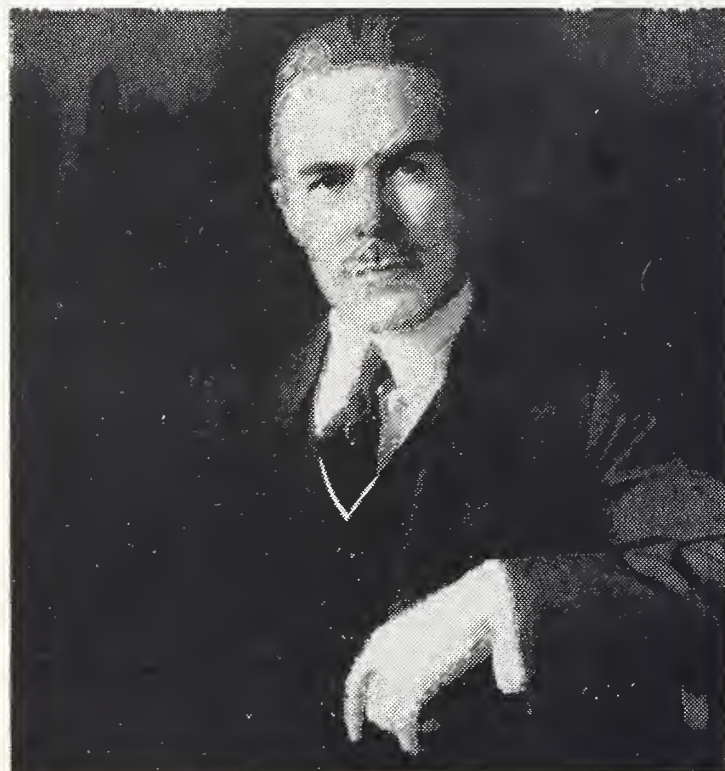


Fig. 1 — William Carpenter MacCarty, M.D.

\*History of Medicine Librarian, Mayo Clinic, Rochester, Minnesota.

†Librarian, Mayo Medical Library, Mayo Clinic, Rochester, Minnesota.

Read at the meeting of the American Osler Society, Kansas City, Missouri, May 9, 1978. Copyright 1978 Mayo Foundation.



medical history to his colleagues, assistants, Fellows, and visiting doctors.

In his lecture notes, MacCarty gave nine reasons for his interest in the history of medicine. He wrote:

1. It teaches me to appreciate the difficulties which it is necessary to overcome in order to succeed.
2. It teaches that great reforms are usually extra mural.
3. It teaches me to evolve rather than spring up.
4. It teaches me not to be fixed in my worship of authorities.
5. It teaches me that great reformers arise out of new conditions or opportunities.
6. It teaches that there is phylogenetic evolution of thought, language and ideas.
7. It unifies mankind and makes the individual a citizen of the world of both the present and the past.
8. It teaches me to see possible and probable events of the future.
9. It gives me courage to use my own faculties and opportunities.

He traced the evolution of medicine through 14 periods:<sup>3</sup>

1. Period of simple reflexes (from creation to the present).

2. Mystical or demoniacal period (at least 4000 B.C. to present).
3. Symptomatic or systematized observational clinical or scientific period (500 B.C. to present).
4. Dark Ages (200 A.D. to 1200 A.D.).
5. Period of gross human anatomy (1200 to present).
6. Microscopic period (1677 to present).
7. Tissue period (1771 to present).
8. Period of cellular anatomy.
9. Embryological period (circa 1870 or 1880 to present).
10. Bacteriological period (1873 to present).
11. Serological period (1889 to present).
12. Chemical period (organic).
13. Biological period (heredity).
14. Physical period (colloid physics, etc.).

MacCarty never published these lectures. But the importance he gave to the study of medical history can be seen in several of his articles. In 1924, when speaking of the status of his own specialty within the profession, MacCarty enlarged on the development of medicine as a whole:

“The vocation which we call medicine is a mixture of art, some science, philosophy, religion, and commercialism (in its broad sense). It is not an art, a science, a

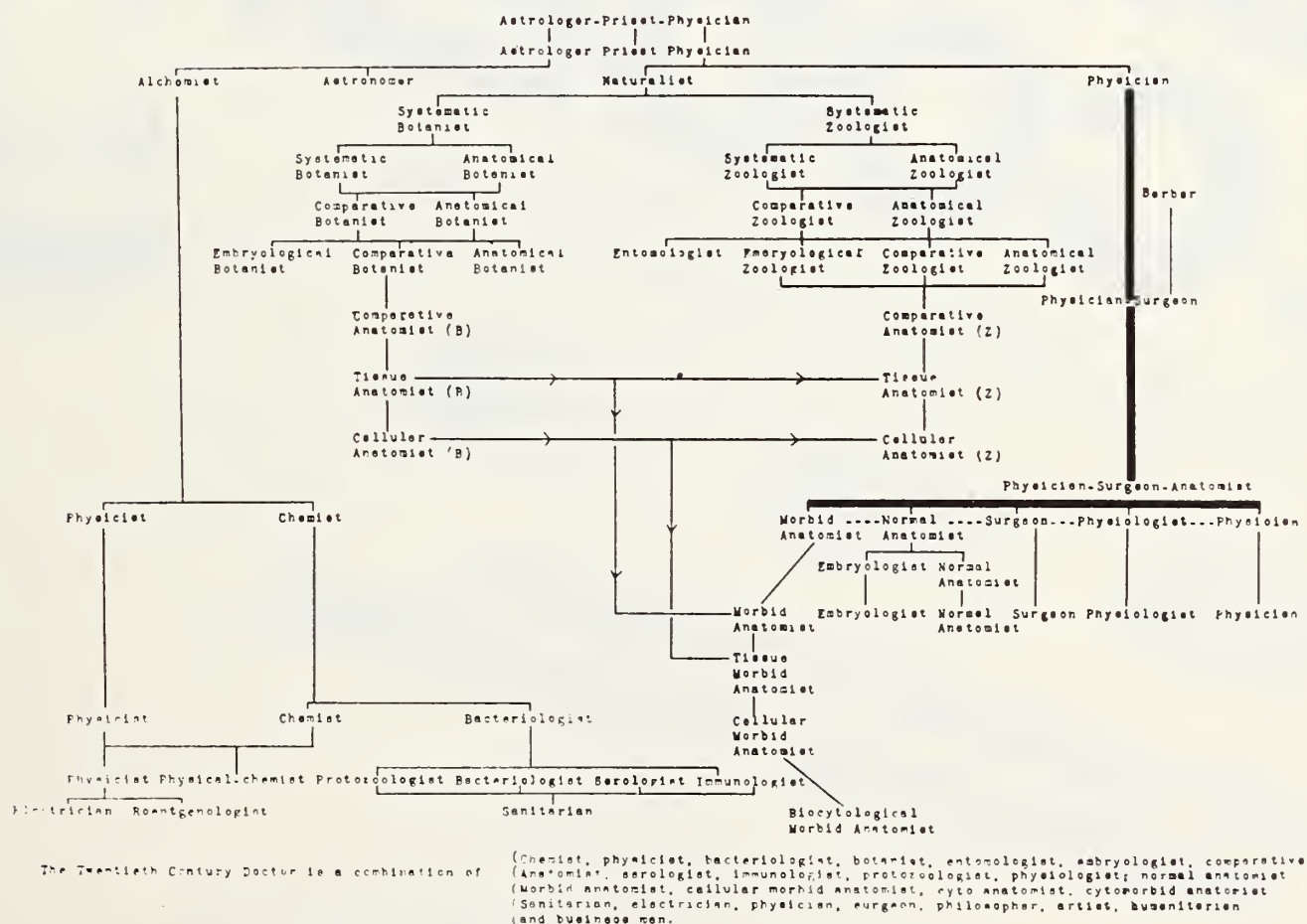
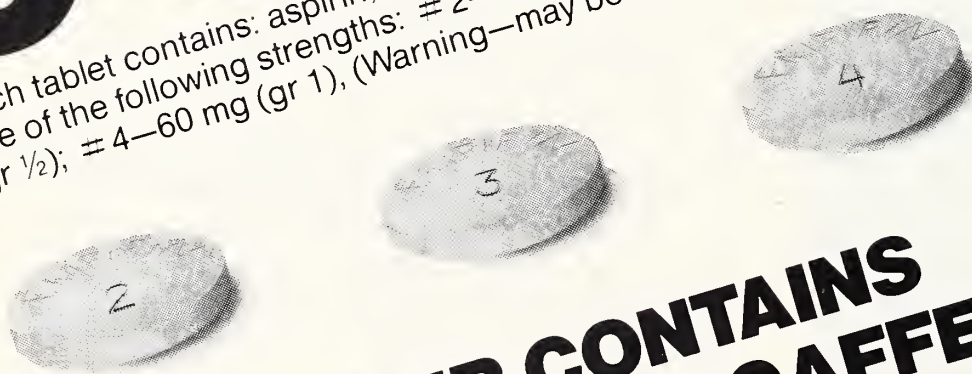


Fig. 2 — The historic development of the doctor. (From MacCarty WC: The making of a doctor. *Ann Clin Med* 2:392-408, 1924 by permission.)



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philosophy, a religion, or a business. It involves research, teaching and the practical application of facts to the individual suffering from disease. As a vocation it is of increasing economic value to our social organization. As a specialty, medicine has evolved out of the functions of the ancient priesthood. Its growth has been slow; its greatest progress has been dependent upon periodic increases in our knowledge of anatomy, physiology, and morbid anatomy, and the application of this information to the recognition, treatment, and prevention of disease. There has been no period when our knowledge may be spoken of as fixed; it is, therefore, not to be classed with mathematics and physics which perhaps represent our most fixed knowledge. It is, as a branch of knowledge, a mass of things — some of which are true, mixed with things which may not be true; it is clothed in a language not universally intelligible even to those who are designated Doctors of Medicine; it is unintelligible to biologists despite the fact that it is a biologic science. It has rapidly grown from a specialty, the functions of which were carried out by a single individual to one, the functions of which involve knowledge of chemis-

try, physics, bacteriology, botany, entomology, embryology, comparative anatomy, serology, immunology, protozoology; physiology, normal gross anatomy, morbid gross anatomy, histology, histomorphology, cytoanatomy, cytomorphology, sanitation, electricity, surgery, philosophy, art, and business.<sup>4</sup>

He reiterated this idea in chart form in a discussion of medical education (Figure 2).<sup>5</sup>

But perhaps his greatest concern in the history of medicine had to do with the "enthusiastic young scientific men" of his own institution and his conviction that "... it should serve them well to study the lives of those whom they consciously or unconsciously emulate."<sup>1</sup> It was because of this concern that he gave his lectures, and his effort brought results. It was after one of these lectures that he was asked by a Fellow in medicine, Dr. James Arthur Buchanan (1887-1950), about the possibility of establishing a medical historical society.<sup>2,6</sup> MacCarty endorsed this suggestion with enthusiasm, and agreed to become the organization's permanent president if the meetings would be held at his home and if the

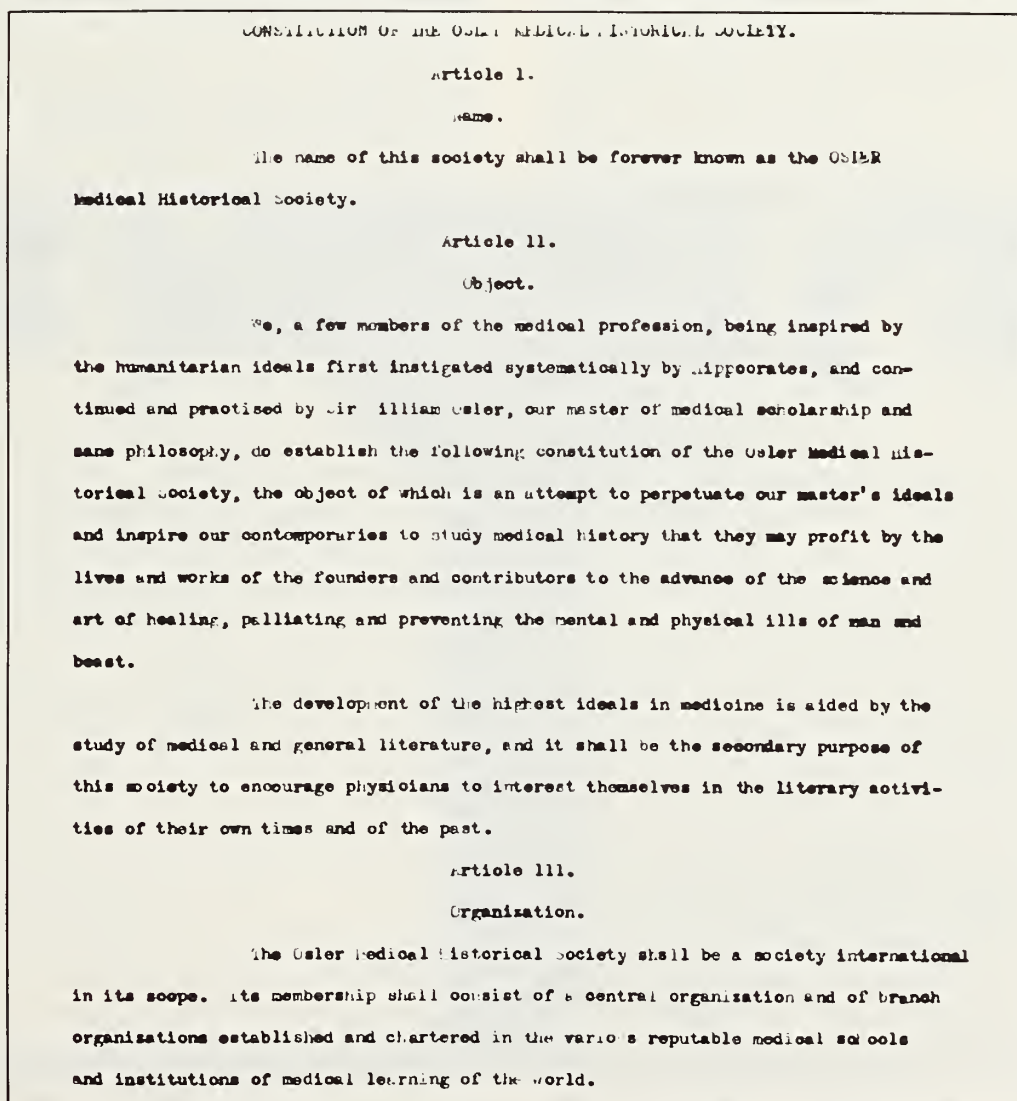


Fig. 3 — Constitution of the Osler Medical Historical Society.



organization were called "The Osler Medical Historical Society." This name for the Society was inevitable, for MacCarty had come under the spell of Osler as a student at Johns Hopkins University. During his postgraduate experience in Germany he wrote his father, "I would rather have been a student of Osler than any other man I ever heard of and every day his greatness and simplicity present themselves stronger and stronger . . . Dr. Osler as the German says, is 'my weak side.' " (Letter from W. C. MacCarty to his father, dated March 12, 1905.)

An organizational meeting was held August 28, 1920. Fourteen physicians attended. The original members were: William C. MacCarty, James A. Buchanan, William C. Chaney, Henry W. Woltman, Merle R. Hoon, Oliver C. Melson, William DeP. Inlow, John B. Doyle, John E. McCorvie, H. Olding Foucar, Charles H. Heacock, Duncan Parham, Alfred S. Giordano, and Harry L. Parker.

In 1921, Gordon S. Foults, John H. Lyons, Walter D. Shelden, Thomas D. Moore, Frank S. Schoonover, Jr., and Arlie R. Barnes were elected to membership. Kenneth S. Davis, Albert S. Crawford, Winchell McK. Craig, and N. C. H. Bull joined the Society in 1922. Benjamin H. Hager, Carl H. Greene, Philip S. Hench, Edward P. Cathcart, and Mynie G. Peterman became members in 1923. In 1924 only two men joined: Louis S. Faust and Theodore S. Swan. The last

persons to join were Stanley H. Mentzer, Gilbert C. Anderson, Christian J. Rohwer, Wendell A. Killins, and James R. Learmonth in 1925.

All of these men voluntarily sought membership in the Society because of their interest in the history of medicine.

At the first meeting, work was begun on a constitution (Figure 3), and the Society was legally incorporated. Dr. MacCarty became the Society's permanent president and Dr. Buchanan, its first secretary.

According to the Constitution of The Osler Medical Historical Society, the object of the Society was to perpetuate Osler's ideals and to inspire contemporaries to study medical history that they might profit by the example of the lives and works of the founders and contributors and further the advance of the science and art of healing, palliating, and preventing the mental and physical ills of man and beast.

It was stated that "the secondary purpose of this Society shall be to encourage physicians to interest themselves in the literary activities of their own times and of the past."<sup>7</sup> Included in the Constitution was the provision for establishing similar societies throughout the world.

Unfortunately the available minutes of the Society do not begin until the meeting on June 23, 1921. The minutes for this meeting contained Buchanan's

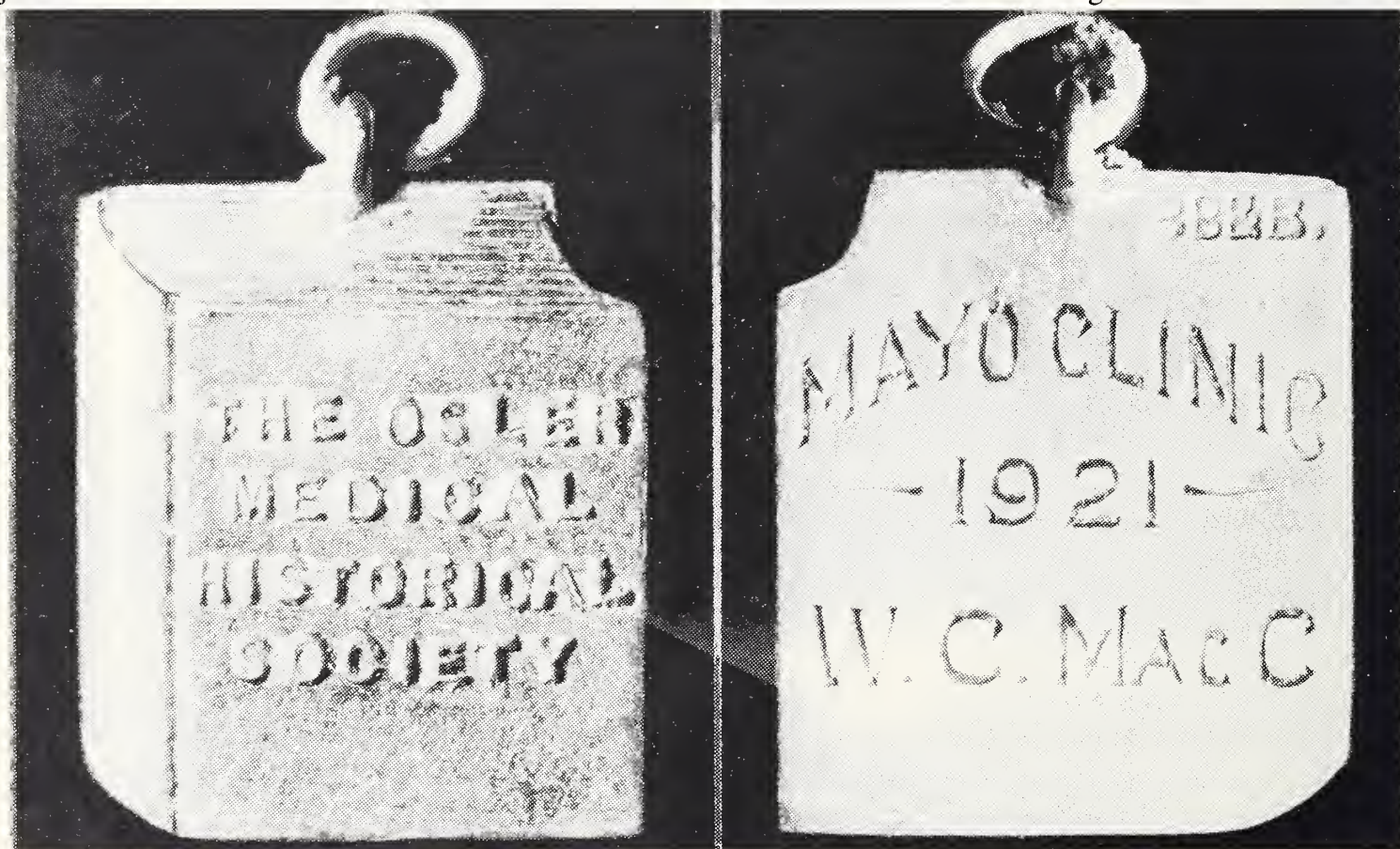


Fig. 4 — (Left) Obverse — Osler Medical Historical Society emblem. (Right) Reverse — Osler Medical Historical Society emblem.



suggestion: "... that it would be advisable to appoint one man to take up the work on establishing the Osler Society in the leading medical schools of the country." This idea was discussed at length at the meeting on July 28, 1921. It was decided that letters should be sent out by Dr. MacCarty to those men of the various schools who were particularly interested in the study of medical history. The first letters were to be sent to Minnesota, Western Reserve, Harvard, Pennsylvania, Dublin University, Syracuse University, Michigan, Western University, University of Indiana, Iowa University, Jefferson, John Hopkins, University of St. Louis, Tulane, University of Louisville, University of Cincinnati, University of Virginia, and Rush Medical School.<sup>2</sup>

Members of The Osler Medical Historical Society were apparently unaware that The Osler Society at McGill had had its inaugural meeting on April 26, 1921.<sup>8</sup>

At the meeting on August 11, 1921, the members decided that many of the papers presented were excellent and should be published. The President assigned the editorial work involved in preparing the papers for publication to Dr. Hoon. Five of the presentations were published.<sup>9-13</sup> Several others were published in later years but without acknowledgement to the Society.

Under the auspices of the Society, at least two visiting lecturers gave public addresses at the Mayo Foundation. Dr. C. P. Howard gave a lecture entitled "Personal Reminiscences of Sir William Osler" on December 30, 1921, and Dr. A. F. Jonas spoke on "The Papyrus Ebers" on June 30, 1922.

It is regrettable that the proceedings of the October 13, 1921, meeting were not recorded in greater detail. After Dr. A. S. Giordano presented a paper on the life of Pasteur, members discussed the question of whether or not there were as many opportunities for the medical investigator of their day as there were for such investigators during the time of Pasteur. It would be interesting to know if a conclusion was reached.

At the meeting on January 2, 1922, Dr. MacCarty's letter to the medical schools was approved. The emblem of the Society, a small gold charm of a book (Figure 4), was also approved.

Drs. Moore and Buchanan were appointed to the committee charged with design of an appropriate certificate (Figure 5). On Apr. 25, 1922, the Society held a farewell dinner meeting at the Zumbro Hotel, in honor of Dr. Buchanan. Members who left Rochester were presented a copy of Osler's *Aequanimitas*

### The Osler Medical Historical Society

To all who read: Be it known that on the  
twenty-eighth day of August 1920

**William Carpenter MacCarty**

Being interested in Historic Lore pertaining to Medicine  
and Surgery was admitted into the Fellowship of the Osler  
Medical Historical Society

Mayo Clinic Chapter



*W. C. MacCarty* President  
*A. H. Buchanan* Secretary

Fig. 5 — Osler Medical Historical Society Membership Certificate.

autographed by members of the society.

In response to an appeal from John C. Hemmeter to Dr. MacCarty, the members voted on March 22, 1923, to send 10 dollars (\$10.00) to help cover the deficit of Sudhoff's *Archiv für Geschichte der Medizin*.

The Society held an annual picnic as close to the birthday of Sir William Osler, July 12, as possible. In 1923 it was held at Frontenac. The program was made up of three parts: a big dinner, a program in the woods, and a swim. After papers on Osler, each member and guest received a small picture of Sir William.

Occasionally at the evening meetings members would be called on for extemporaneous speeches. Some examples of these presentations noted in the Society minutes were: "The Obstetrical Hand," "Neurology, Coordination and Automobiles," "The Fair Sex of Vienna," and "The Effects of Prohibition on the Incidence of Overdistention of the Bladder."

Two of the members of this early Osler Society (Dr. H. O. Foucar of London, Ontario, and Dr. Benjamin H. Hager of Indian Wells, California), in response to our letters concerning this paper, recalled how much they enjoyed the meetings at the MacCarty home — the formal papers and the lively discussion that followed — all accompanied by apple cider and sociable smokes. Dr. Foucar mentioned that absenteeism was rare and that each member chose his own topic and gave it a great deal of serious thought and study. As an example, he mentioned one paper that he had presented — a paper on Dr. Edward Livingston Trudeau and his work. The bibliography consisted of 99 titles including a review of all Trudeau's publications, his autobiography, biography, memorial addresses, editorials, and so forth. "The Society was stimulating intellectually and enjoyable socially. It was one of the oases in my life." Dr. Hager stated that "Every meeting was a



joyous occasion. We, the members, were such good friends with mutual interests that the evenings together were always a great event.”

According to the minutes, the Society held 66 meetings between June 23, 1921, and July 3, 1925. But this convivial fellowship could not survive the realities of a changing population of fellowship staff and the increasing professional responsibilities of those members who remained as the Mayo Clinic Staff. It became too difficult to maintain regular meetings. The last meeting was held July 3, 1925.<sup>2</sup>

Documented is the fact that the Mayo Foundation “Chapter” of the Osler Medical Historical Society was initiated on August 28, 1920. Thus it may very well be the earliest named Osler Society of its type in the United States. Rosencrantz,<sup>14</sup> under the subject heading, “Orations and Lectures,” pointed out that an “Osler Memorial Association of Los Angeles . . . was established about 1920 by a group of physicians in the vicinity of Los Angeles. The first lecture, given by Dr. J. T. Finney in 1921, was ‘A Personal Appreciation of Sir William Osler.’ The association was short-lived.” (Since the first lecture was given in 1921, it is probable that the group organized late in 1920.) Rosencrantz,<sup>14</sup> under the subject heading “Clubs and Societies,” noted

In January 1896, in order to raise money for the library of the Medical and Chirurgical Faculty of Maryland, a book and journal club was organized at Osler’s home, with Osler as president. By the following year the programs were entirely devoted to papers on the history of medicine . . . In 1929, the name was changed to the Osler Historical Club. . . .

The Mayo Foundation “Chapter” predates by eight

months the McGill Osler Society in Montreal. However, there was an Osler Reporting Society at the Royal Victoria Hospital in Montreal which was formed about 1920. Its constitution states “. . . founded 1921 in Montreal.”<sup>14,15</sup>

Priority among these may be moot anyway, as there appears to have been an Osler Society at Queen’s University in Kingston, Ontario, that dates back to at least January 13, 1916.<sup>16</sup>

The Osler Medical Historical Society was the first of three societies on medical history at the Mayo institution. In 1927 the Salerno Club was organized by Fellows of the Mayo Foundation. This organization held meetings until 1936. Shortly after World War II an abortive attempt to found another society was made, but only one meeting was held. The Mayo Foundation History of Medicine Society was organized on March 12, 1964, and continues to function.<sup>17</sup>

The desire for unity with the past is often felt by the physician. Knowledge of development in the limited area of his own specialty he has by necessity. But the search for the good, inherent in the physician’s quest, makes him seek for figures from the past who had an affinity with the greatest purposes in his profession: Aesculapius was a god, Hippocrates a father, Galen an authority, Avicenna a prince. The 20th century scientific physician has Osler to guard his ideals, foster his humanity, and join him in mental union with like-minded individuals through the centuries. Through his student, W. C. MacCarty, Osler’s influence toward a humanistic study of medicine was manifested at the Mayo Clinic during its early years.

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# Guest Editorial

## Who Will Practice Medicine In the 80s?"

Medicine and all of its branches are under attack by paramedical and non-paramedical groups who are trying to lower the standard of licensure so they may practice medicine even though they have not achieved the proper qualifications. Each success serves as a precedent to the invasion of the practice of other branches of medicine by such groups.

One type of strategy by which non-medical groups hope to attain medical status was clearly revealed when in 1978 Optometry launched a multi-million dollar nationwide advertising campaign. Ads, directed toward an unsuspecting public, stated that "an examination by an optometrist is also a good place to begin guarding your family's total health care". They concluded this advice to bypass the general medical practitioner, the internist and the pediatrician as well as the ophthalmologist by proclaiming, "Your Family Doctor Of Optometry, The Person To See and Continue Seeing".

Optometrists have also succeeded in obtaining by legislative fiat the license to use so-called diagnostic drugs in 21 states and *therapeutic* as well as diagnostic drugs in 2 states. Recent legislation, proposed in Arizona, would have permitted these same non-medical practitioners to perform surgery on the eye.

Minnesota Ophthalmologists believe an "optometric drug bill" will be proposed in the 1980 legislative session. This foot-in-the door type of legislation from non-medical personnel must be stopped, or *all* physicians and their patients will suffer.

This legislation should be opposed because:

- Drugs are unnecessary for a full and adequate optometric examination.

- Optometrists lack adequate medical and clinical training in the use of drugs.
- The diagnosis of disease for which the drugs may be used is beyond the scope of optometric practice.
- The public health and welfare could be adversely affected by improper use of these drugs, while no significant improvement may be obtained by the proper use of drugs.
- Increased optometric services will require additional charges by optometrists, in part to cover potential increases in malpractice insurance rates for optometrists who use these drugs.

If such a decline of ophthalmic standards spreads nationwide, it would threaten ophthalmology as a recognized medical specialty and would establish a precedent fraught with grave danger for all of medicine. It would provide both legal sanctification and momentum to nurse-practitioners, chiropractors, and non-medical technicians who seek to obtain by legislative fiat what they have failed to obtain by degree.

Each of us must act now. Contact your legislators, particularly those on the Health and Welfare Committees. Also inform legislative candidates on this issue. Explain the dangers to the public health of expanding the scope of practice of the optometric industry beyond the optometrists' capabilities.

If we don't present our case, we may lose. If ophthalmology loses, all of medicine loses. To emerge victorious, we need the support of all physicians in 1980 and thereafter.

Please help us prevent laws which would license non-medical personnel to practice medicine.

Raymond C. Croissant, M.D.  
President

Minnesota Association of Ophthalmology

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# MMA ANNUAL MEETING

MAY 20-22, 1980

Dear Fellow Minnesota Medical Association Members:

Your Association Subcommittee on Scientific Assembly is pleased to present the 1980 Annual Meeting Continuing Medical Education Program for your consideration. The Subcommittee has attempted to be innovative and to maintain the Association's tradition of presenting quality courses that are relevant to our practices. We believe the courses offer a diversity of application and present something of interest for all practitioners.

The site of the 1980 Annual Meeting is the Radisson South Hotel in Bloomington. Recognized as a preferred Minnesota setting for an event such as our Annual Meeting, this facility offers a readily accessible location and superior accommodations.

Maintaining our previous mode, the CME Program emphasizes subjects relating to clinical medicine with a sprinkling of non-clinical but practice-related sessions. All are designed to enhance our skills in patient management in a stimulating and enjoyable manner. The success of an innovation in the 1979 session encouraged us to schedule three off-site courses in hospital settings to provide learning experience not possible in the hotel.

Scheduling follows last year's format of courses from 8:30 a.m. to 11:30 a.m. and 2:00 p.m. to 5:00 p.m. The extended noon hour intermission will provide you with ample time to explore our exhibits. We urge that you do so and demonstrate appreciation for the exhibitors' support of our program.

You will also enjoy the Third Annual Meeting Reception to be held from 7:00 p.m. to 9:00 p.m. on Tuesday, May 20, in the exhibit hall. Complimentary hors d'oeuvres and a cash bar will be available. Our Luncheon speaker on Wednesday, May 21 will be Howard G. Wilcox, M.D., a medical historian from Salt Lake City, Utah. Dr. Wilcox will speak on little known and interesting aspects of the medical histories of selected American Presidents.

Early registration is important to assure that space is reserved for you in the courses of your selection and that instructional material can be prepared in advance for each participant. The program is fully accredited for CME credit (Category 1 AMA with Prescribed AAFP requested).

The Subcommittee on Scientific Assembly extends a most cordial invitation for you to join us in Bloomington for an exciting meeting.

Sincerely,



Robert F. Avant, M.D., Chairman  
Subcommittee on Scientific Assembly

P.S. Don't forget, this year's program will be held on Wednesday and Thursday, May 21 and 22.



# from Division of Socio-Economic Affairs

James H. Sova, Assistant Executive Vice President  
Lynn R. Gruber, Director, Department of Medical Services and Research  
George C. Lohmer, Jr., Director, Department of Health Planning  
Charles W. Wiger, Director, Department of Legislative Affairs

**With this issue, we are initiating this special section highlighting some of the activities of the MMA Division of Socio-Economic Affairs.**

**Future issues of the Journal will contain information relating to socio-economic affairs of interest to physicians on a regular basis.**

**James H. Sova**

## Legislative Affairs

Minnesota's 201 state legislators wrapped up one of the most bitter and political sessions in memory at 4:00 a.m. on April 12, 1980. After returning for ceremonial "sine die" adjournment just six hours later, the legislators raced home to their districts where all but about 20 of them seek re-election. At home legislators face constituents challenging them on particular votes. MMA reported legislative action and votes of significance to medicine in the Physician's Legislative Bulletin for you to use as a guide in evaluating your legislator. The end-of-session issue was sent recently to all MMA members.

In state lawmaking, as well as many other areas, the following principle holds true: *those who get involved and speak up usually run the show*. Your MMA Committee on Legislation and staff have seen this principle affirmed every legislative session. For example, at the recent 1980 session, many physicians and auxiliaries were actively involved. This involvement led to legislators responding to MMA concerns as follows:

- Establishing a statewide poison information center that was sponsored by the MMA.
- Rejecting moves to mandate chiropractic and optometric services in HMOs.
- Including a 24-hour advance notice to MDs when the Welfare Department seeks access to medical records.
- Establishing legislative authority for MMA to form a self-insurance trust for malpractice coverage.
- Including medical records as private documents under the state data privacy law.
- Rejecting any expansion of the Certificate of Need Act.
- Deferring action on major HMO revisions and changes in the Hospitalization and Commitment Act.
- Rejecting a proposal for psychosurgery regulation (MMA voluntary guidelines were deemed adequate).

The list goes on. The Minnesota Medical Association had a very successful year. But success is fleeting, and we now look to the 1980 elections. Returning legislators who support MMA is important in assuring a successful 1981 session.

### MMA Physicians Provide Blood Pressure Testing/Screening Program for Legislators

During the tense, closing weeks of the legislative session, several MMA physicians volunteered their services at the Legislature to provide blood pressure testing and screening for legislators and staff. The program, which came in response to a request from the Minnesota Senate, was very well received. Besides getting their blood pressure taken, legislators were given helpful background materials regarding stress, diet, and smoking. Some legislators were referred to their personal physician for follow-up. Physicians participating in the program included as follows: former state legislators, Dr.



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### Medical Services and Research

#### Increase in Physician Reimbursements for Welfare Patients

As a result of discussions between Governor Al Quie, Arthur Noot, Commissioner of the Department of Public Welfare (DPW) and Minnesota Medical Association's leadership and staff, DPW has just announced increases in provider reimbursement for practitioners serving medical assistance (MA) recipients for services occurring on or after July 1, 1980. Starting in July, reimbursement will be based on 1978 charge data. Currently provider reimbursement is based on 1976 figures.

In other news from Minnesota's Department of Public Welfare, it was recently announced that Minnesota's MA Program must pay for abortions which are medically necessary as determined by the woman's attending physician in light of all relevant factors, including: physical, emotional and psychological conditions, and the woman's age.

The change of policy results from action by Federal courts in New York and Minnesota.

### Health Planning

#### Proposed Con Regulations Out in Draft Form

The Minnesota Department of Health has issued draft Certificate of Need regulations. These regulations are designed to cover physician purchases of expensive office equipment if used for hospital inpatients. MMA staff is closely monitoring the development of these proposed regulations.

#### State Health Plan Approved

After three years of work, the Statewide Health Coordinating Council at its recent meeting approved Minnesota's first State Health Plan (SHP). The SHP is the single most significant document on the health care system in the state, setting the direction and policy for a system which affects all of Minnesota's citizens, patients, hospitals, and physicians. The MMA testimony on the SHP, given at the March 5, 1980 public hearing on the Plan was generally incorporated within the Plan.

#### VA Hospital in Minneapolis Plans a Replacement

The Veteran's Administration Hospital in Minneapolis is planning to expand through a major renovation on its Fort Snelling site. This proposed project must be reviewed by the Metropolitan Health Board (the local HSA) who will then send their recommendation to the U.S. Congress.

The MMA has taken the following positions:

1. That the significant medical contribution of the VA Hospital in our community be recognized.
2. That the VA proposal be reviewed through a Certificate of Need process on the local level (thus the VA proposal would be treated the same as any other hospital building program).
3. That efforts be made to parallel the renovation and expansion plans of the VA and University of Minnesota Hospitals so as to reduce the potential for duplication.
4. Explore the possibility of extending PSRO activities to the VA Hospital.

A preliminary hearing was held by the Senate Veteran's Affairs Committee in Washington, D.C. to discuss the Minneapolis VA proposal on April 8, 1980. The MMA was represented by A. Stuart Hanson, M.D., the Chairperson of the Physicians Metro Health Force (PMHF). Dr. Hanson replaced John B. Coleman, M.D. as Chairperson of the PMHF January 1, 1980 for a two year term. Dr. Hanson stressed our past participation in health planning, as well as raising some issues to be discussed by the Senate VA Committee.



## Classified Advertisements

Classified advertising rates are forty (40) cents a word; minimum monthly charge \$10.00, key number, \$1.50 additional. Replies to advertisements with key numbers should be mailed in care of Minnesota Medicine, 101 East 5th, Suite 900, St. Paul, Minn. 55101.

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# President's Letter



Although we in medicine are understandably concerned about the immediate and future problems of our profession, I believe it behooves us on occasion to examine our past and search for our roots.

Not long before I succeeded to the presidency of your Association, I reviewed some aspects of its history and in particular the history of the presidency. The Minnesota Medical Association (The Minnesota State Medical Association) was founded in St. Paul one hundred and twenty-seven years ago in 1853 by eleven physicians. I represent the one hundred and thirteenth president of the Association. This discrepancy is accounted for by the fact that the first president, Dr. Thomas Reid Potts, served sixteen years, and the second, Dr. Samuel Willey, served two. There were two instances where two men were listed as serving in the same year, presumably due to death or resignation.

Many of the names on the roll of the presidents of this Association are familiar to me. Most of the recent occupants of this office I am well acquainted with.

Our past does not seem so long ago when I note that I can well remember meeting the twenty-sixth president of the Association when I was a small boy and my father was serving as president of the Southern Minnesota Medical Association. Even then I realized that I was in the presence of legendary physicians when I was introduced to Dr. W. J. Mayo and his brother, Dr. C. H. Mayo, another previous occupant of this office. An organization where the one hundred and thirteenth president can remember meeting the twenty-sixth president must have an element of continuity that is significant.

St. Paul provided twenty-eight presidents, Minneapolis twenty-five, and Rochester fifteen. Eight previous presidents have been from Duluth and four from Winona, the city in which I grew up. Three of the first twenty presidents of the Association were from Winona, which would appear to represent evidence of the interest of that city's early physicians in the fledgling Association. Dr. Franklin Staples of Winona, the third president, was a man of considerable distinction. He became Vice-President of the American Medical Association and was a longtime member of the Minnesota State Board of Health. He was also a founder of the Winona Preparatory Medical School and for a time held a chair in the Medical Department of the University of Minnesota.

The most recent president of this Association from Winona was Dr. R. H. Wilson who served in 1956. I knew him very well when I worked as an orderly in the old Winona General Hospital.

Dr. B. J. Branton was the only previous physician from Willmar to serve as president of the Minnesota Medical Association. Dr. Branton had died before I began practice in Willmar, but through the years I have seen many of his old patients and heard much about him, so he seems a very real person to me.


Among the names on the list of presidents of this Association are those of: Justus Ohage, George Earl, E. M. Hamnes of St. Paul; E. Starr Judd, A. W. Adson, Louis A. Buie of



## PRESIDENT'S LETTER

Rochester; H. B. Sweetser, Donald McCarthy of Minneapolis and E. L. Tuohy of Duluth. The contributions of such men as these to medicine and to this Association are well known.

For me this excursion into the past has not simply been one to evoke memories, but it has served to confirm for me the fact that our Association has been constituted through its long history of dedicated physicians who have searched for the best avenues to improve and maintain the health of the citizens of our state. We must continue in their footsteps.



**John K. Meinert, M.D.**  
**President**  
**Minnesota Medical Association**

---

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In 1978, the Minnesota Legislature passed legislation that required the Minnesota Department of Health (MDH) to institute fees for laboratory services. Since July 1, 1978, there has been a \$1.50 handling fee per specimen. Handling fee stickers are available for purchase on a pre-paid basis. Some of the services of agencies that receive Federal or State funds administered by the MDH may be exempt from the handling fee, and some categories of specimens are exempt from the handling fee.

The MDH Medical Laboratories are still receiving specimens without the required handling fee stickers. We are considering actions, as of March 1, 1980, such as holding specimens (or test results), when specimens (for which no exemption from the handling fee has been established) are received without the handling fee sticker. Submitters will be notified about specimens being held, and one handling fee sticker per specimen will be due when notification is necessary.

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# Candidacy



Robert T. Kelly, M.D.

Dr. Robert T. Kelly, after a long career in medical affairs in the Range County Medical Society, the Minnesota Medical Association, and the AMA, is a candidate for the Board of Trustees of AMA.

Bob has served as an AMA Alternate Delegate and Delegate for twelve years in the House and chaired the MMA delegation. He was elected to the Council on Medical Service in 1974 and was recognized there for his leadership by being elected successively Vice-Chairman and Chairman of that Council. He headed an ad hoc committee on PSRO of the Council. He is a member of the National PSRO Advisory Council; served on the AMA Speaker's Bureau; and chaired the Ad Hoc Committee on Practice Evaluation.

He is former President of the North Central Medical Conference.



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## Editor's Notebook

### Where Have All the Flowers Gone?

*"Where have all the flowers gone? Long time passing.  
Where have all the flowers gone? Long time ago.  
Where have all the flowers gone?  
Young girls picked them, every one.  
Oh, when will they ever learn?  
Oh, when will they ever learn?"*

Song, *Where Have All The Flowers Gone?*  
Words and Music by Pete Seeger, 1961

Flowers come in all sizes, any colors, in varying seasons, and with unique, changing, and complex characteristics. They come tall, short, skinny, and plump. There are glorious and anemic ones, bold and shy ones, adventuresome and retiring ones. All differ. Roses may be red, and violets may be blue, but dandelions get around more than the others do.

Whatever their characteristics, flowers symbolize hope, optimism, renewal, beauty, and life.

Indeed, we celebrate life with flowers. On my farm hangs a plaque. The plaque proclaims: "Don't worry, don't hurry, and don't forget to smell the flowers." I don't forget, for flowers are what it's all about.

We reward deeds well done with flowers. What do you give a diva to show how much you appreciate her aria? How do you tell people you care for them? With flowers, of course. I recall a sage old Connecticut practitioner. When asked why he and his wife of fifty years hit it off so well, he confessed: "I send her flowers every Saturday to celebrate another week."

Where have all the flowers gone in our society? Why don't we send flowers anymore?

This is an anti-hero age. We no longer offer bouquets to celebrate hope, optimism, beauty, life, and achievements.

Instead we doubt, dissect, disparage, analyze, impugn, question, and investigate.

Boy, do we investigate. We investigate Presidents, Congressmen, Senators, Supreme Court Justices, Priests, Physicians, and Establishment Institutions. The prevailing attitude is: if *they* or *it* have succeeded in our society, something *must be* wrong. After all, our most prominent heroes, even Muhammad Ali, have feet of Clay. So we send no flowers, only regrets that things are not perfect.

"Investigative" reporters "reveal" to us what we know already — that our leaders and the organizations they manage suffer from human frailties. The reporters astonish us with mundane disclosures: Presidents dislike their political enemies. Congressmen appease, and even try to please, their constituents. Supreme Court Justices, heaven forbid, actually argue among themselves about controversial cases. The Justices even maneuver in their cloakrooms to win their brethren over to their point of view. Goodness, these learned lawyers act like they are made of flesh and blood. No flowers are bestowed upon them for their lifetimes of hard work and solid accomplishments.

And physicians?

Well, they are the worst. Imagine. They err like other mortals. They occasionally misinterpret signs, symptoms, and results. They cannot guarantee perfect results under all circumstances. They cannot even repeal the Laws of Nature. Physicians, to sum up, are not



## WHERE HAVE ALL THE FLOWERS GONE

omnipotent or omniscient.

In *Heart Sounds*, a current bestseller, Martha Lear has a complaint: Physicians did not save her urologist husband, Doctor Harold Lear, from death from coronary disease. Yes, the doctors tried a coronary bypass and other technologies. But they did not reverse Nature's already flowing tides in Doctor Lear's body — his miserable family history of early death from coronary disease, his persistently high serum cholesterol, his thirty year history of smoking three packs a day, and the inevitable stresses of moving in middle age from a secure private practice in Connecticut to an uncertain academic (and bureaucratic) career in New York City. Yet Mrs. Lear feels doctors, even when dealing with this stacked deck, should have converted a losing hand into a winning one. She fails to appreciate that man does not always die of disease. He dies of the accumulating consequences of degenerative processes, inherited and acquired during a lifetime. No mixture of the art and science of Medicine, however adroitly applied, will salvage every one from the degenerative diseases.

In any event, she sends no flowers. She makes no mention that the death and complication rate from coronary bypass surgery is now quite low, that most patients are relieved of their anginal symptoms, and that, in selected types of coronary disease, life is unquestionably prolonged.

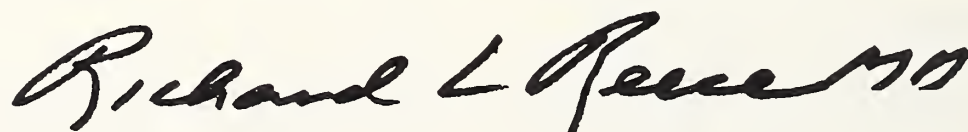
Then there is the current series on the Mayo Clinic in the *Minneapolis Tribune*. The authors reveal to us that this respected institution has succeeded by sticking to its principles, remaining tightlipped, exerting power to protect its own interest, striving for excellence, and playing to strengths of the city and society in which it must live.

The reporters are good at stripping Mayo's petals one by one, but they offer few bouquets, and little acknowledgement that Mayo is an incredible organizational achievement. In rural Minnesota, a big idea — that a large group of physicians can work together and achieve excellence by systematically applying knowledge — was planted 70 years ago. That idea has taken root and flowered into a universally respected, beautifully managed, and remarkably effective institution. But we hear little of this.

Instead, we learn that the Mayo Clinic is "too conservative", as if that were bad, and that, although it "always" gets "high marks", it is "not necessarily the best". It is not, in short, perfect, which means up to the expectations of the reporters. But it *is* extremely effective, as are most of the hardworking, well-educated, and experienced professionals in our society.

Maybe we should praise our professionals and their institutions rather than constantly defoliating them. We are not miracle workers, but given Nature's limitations, we are damn good.

Criticism has its place, but so do flowers.



---

Southern Minnesota Medical Association Meeting  
September 27, 1980  
New Holiday Motel, Mankato



# Multiple Vascular Infarction

## A Manifestation of Sickle Cell Trait in the Absence of Hypoxia

TONI R. MAGNUSON, M.D.\*, SAMUEL W. HUNTER, M.D.†, and RAYMOND C. BONNABEAU, JR., M.D., PhD.†

Patients who are carriers of sickle cell trait hemoglobinopathy (Hgb AS) have been thought to be bearers of a "benign" condition that becomes clinically significant only if they are subjected to conditions of severe hypoxia. Following such episodes, documented systemic abnormalities similar to those occurring in patients with full blown sickle cell anemia (Hgb SS) have been reported.<sup>1,2</sup>

This paper presents a patient with sickle cell trait who exhibited multiple systemic vascular infarctions, without predisposing hypoxia.

A 37-year-old black male came to Bethesda Lutheran Medical Center in 1974 with the chief complaint of recurrent left upper abdominal pain upon exertion. Hemoglobin electrophoresis had shown the patient to be a sickle cell trait carrier (Hgb AS). He had been in excellent health and gave no history of trauma. Physical examination revealed a large non-tender mass in the left upper quadrant of the abdomen. Selective coeliac axis arteriogram and liver-spleen scan (Figures 1A & 1B) revealed the splenic vessels as well as a small rim of normal functioning splenic tissue to be compressed about the periphery of the mass. An upper gastrointestinal series demonstrated the lesion to be extrinsic to the gastrointestinal tract; the stomach and intestines being pushed inferiorly and to the right (Figure 2). Differential diagnosis at this point included a retroperitoneal mass, or a pancreatic or splenic pseudocyst. An exploratory laparotomy was next performed and a 25 × 30 cm., 15 pound pseudocyst of the spleen was removed without

incident. The patient had an uncomplicated postoperative course.

He remained asymptomatic until one year later when the onset of left-sided chest pain occurred. Chest Xray at that time (Figure 3A) revealed a rounded lesion in the lower lobe of the left lung which had not been present one year previously. The patient also had a 30 pack year smoking history. He was readmitted to the hospital where physical examination, routine laboratory studies, sputum, cytology, and bronchoscopy were all found to be normal. An exploratory left thoracotomy with wedge resection of the left lower lobe tumor was therefore carried out. Histological examination showed the lesion to be inflammatory and compatible with a resolving pulmonary infarct. The vessels throughout the area were congested with sickled red blood cells (Figure 3B). The patient made an uneventful recovery and has had no further problems to present.

### Comment

The total red cell hemoglobin in persons with sickle cell trait has been shown to be composed of between 25-40 percent Hgb S, and 55-75 percent Hgb A. The

\*Department of Family Practice and Community Health, Bethesda Lutheran Medical Center, St. Paul, Minnesota and the University of Minnesota Health Sciences Center, Minneapolis, Minnesota.

†Departments of Surgery and Family Practice, Bethesda Lutheran Medical Center, St. Paul, and the University of Minnesota Health Sciences Center, Minneapolis, Minnesota.

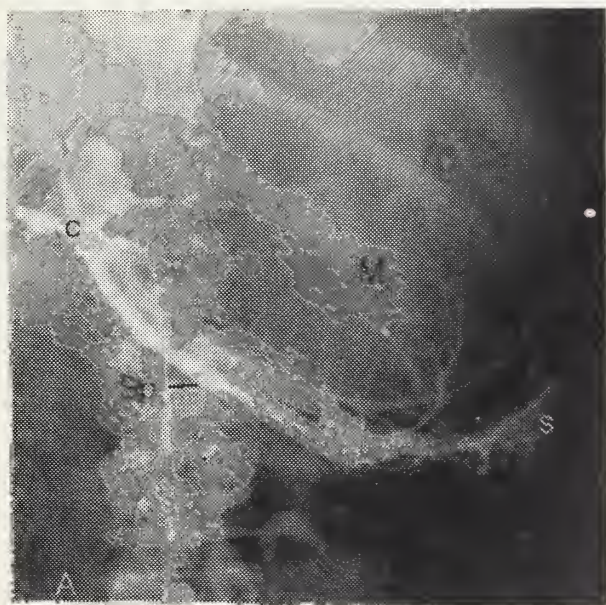


Fig. 1(A) — Selective coeliac axis (C) arteriogram. A large left upper quadrant mass (M), may be seen compressing the splenic artery (SP) and smaller splenic vessels inferiorly. A small rim of relatively normal splenic tissue (S) may be seen. This was confirmed by liver-spleen scan. (See Figure 1B).

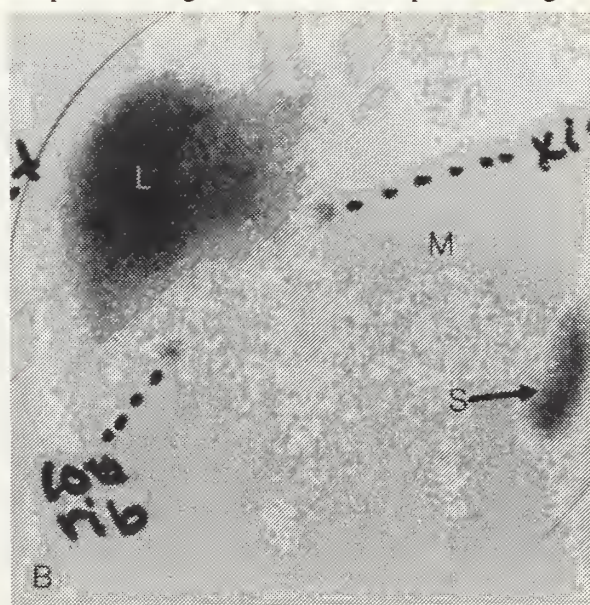


Fig. 1(B) — A liver-spleen scan showed the presence of a small remaining rim of normally functioning splenic tissue (S) compressed by a large space occupying mass (M). The upper dotted line points to the xyphoid process in the patient's midline. The lower dotted line points to the 10th rib on the patient's right, below the liver (L).



tendency for sickling depends upon the relative proportions of each hemoglobin contained in the red cell mass<sup>2</sup>. Cells, therefore, with a proportionally higher percentage of Hgb S are less resistant to sickling than are those who possess a higher percentage of Hgb A. Sickling of red cells in patients carrying the trait alone does not usually occur until the oxygen saturation falls to low levels (below some 30 percent), while red blood cells with full blown sickle cell anemia (Hgb SS), sickle at much higher oxygen saturation (65 percent)<sup>2,3</sup>. Patients with the latter hemoglobin pattern

are able therefore to develop symptoms without the presence of a significant hypoxia. Hypoxia however, had been thought to be necessary for sickling to occur in individuals who are afflicted with only the sickle cell trait<sup>1</sup>. Thus, active red cell sickling has been reported in patients possessing the trait who have been subjected to reduced oxygen tensions during periods of prolonged underwater swimming such as scuba diving, high altitude flying in unpressurized aircraft and during general anesthesia where oxygen levels were not adequately maintained.<sup>1,4</sup>.

True cysts of the spleen (i.e. lined with epithelium) while reported are extremely rare. Echinococcus parasitic infections may result in splenic cysts in less than 2 percent of the infected cases.<sup>5</sup> It is generally felt that the majority of splenic pseudocysts arise from splenic infarcts, the etiology of which may be trauma, splenic torsion, splenic vascular pedicle thrombosis, splenic arterial embolization, pancreatitis or as a complication of sickle cell disease.

In the case under discussion, the presence of sickle cells within the pulmonary lesion and the absence of trauma and other causes, strongly suggests that the large splenic pseudocyst removed from the patient previously, was caused by a splenic infarct or infarcts produced by an active sickling process in a patient who possessed only the sickle cell trait. Since there was also no history of hypoxia, it would also appear reasonable that the possession of the trait alone may not be necessarily a "benign" condition even if predisposing periods of acute hypoxia are absent. These findings lend support to observations recently made by others, where a splenic infarct was documented as the cause of an acute abdomen in a patient with sickle cell trait who



Fig. 2 — Photograph of an upper gastrointestinal series in the patient under discussion, prior to laparotomy. The large mass (M) was shown to be extrinsic to the gastrointestinal tract, pressing the stomach (S) and intestines inferiorly. The lesion at laparotomy was found to be a large, 15 pound splenic cyst.

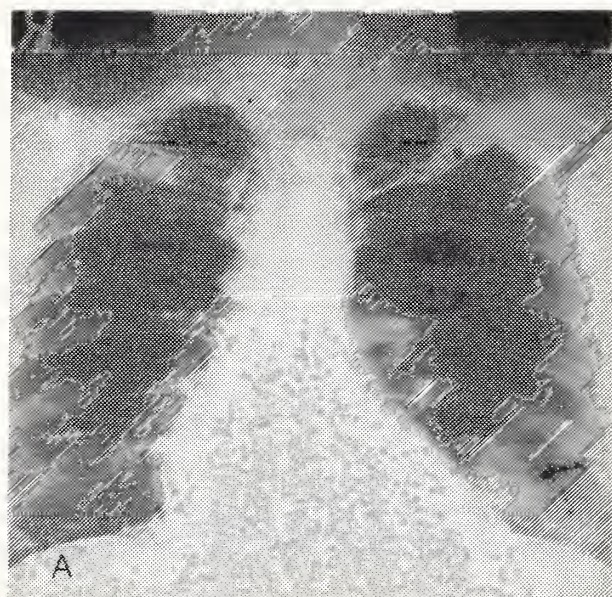


Fig. 3(A) — Photograph of PA chest Xray in the same patient illustrated in Figures 1 and 2, one year after laparotomy and removal of a 15 pound splenic cyst. A rounded lesion (arrow) in the left lower lobe, (not present previously), may be seen.

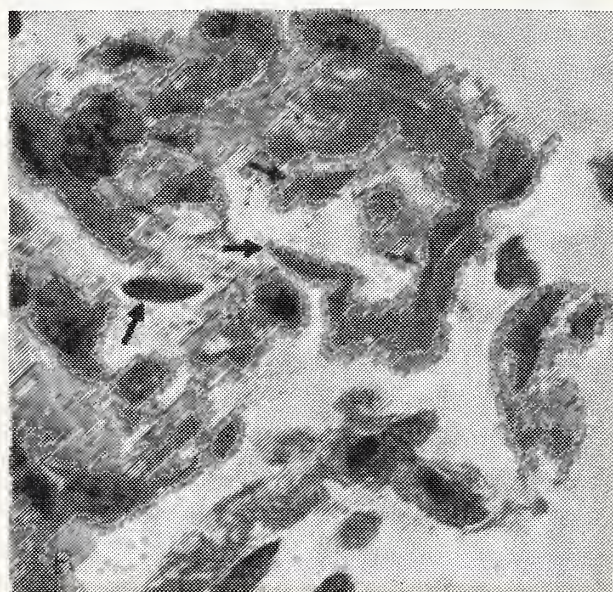


Fig. 3(B) — Photomicrograph (H & E  $\times 900$ ) of the left lung mass removed by wedge resection. Histologically the lesion was inflammatory and compatible with a resolving pulmonary infarction. Multiple sickle cells (arrows) may be seen.



also presented without predisposing hypoxia.<sup>6</sup>

### Conclusion

A case of multiple systemic vascular infarctions (spleen and lung), necessitating a laparotomy, (with

splenectomy) and thoracotomy (with pulmonary wedge resection), one year apart, which appeared related to red cell sickling in a patient with sickle cell trait hemoglobinopathy (Hgb AS) without predisposing hypoxia is presented.

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### Cover Photo

“Northern Minnesota Serenity”

On his way to the Boundary Waters Canoe Area a few miles from Ely, this secluded, rustic and peaceful scene attracted Dr. Freeman D. Kovack's attention. The result was this beautiful cover. The position of the sun and fluffy clouds added to the effect desired by Dr. Kovack.

He is a family practitioner practicing in a group practice in Minneapolis. Dr. Kovack received his medical degree at the University of Vienna and has been practicing in Minnesota since 1952.

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# Hypomagnesemia and Inappropriate Secretion of Antidiuretic Hormone

ALAN F. KREMEN, M.D., PH.D.\* AND ARNOLD J. KREMEN, M.D., PH.D.†

**Case presentation and literature review of a grand mal seizure disorder and the syndrome of inappropriate ADH secretion occurring in a 72-year-old woman with hypomagnesemia. Seizures and metabolic abnormalities responded rapidly to magnesium repletion and fluid restriction. The case stresses the need for monitoring magnesium levels in nutritionally depleted patients.**

**M**AGNESIUM DEFICIENCY has been a neglected abnormality in clinical practice.<sup>4</sup> The following case presents an interesting association between hypomagnesemia and the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). This association has not been reported in the medical literature before. What follows is the case presentation and a brief review of the pathophysiology of each syndrome.

## Case Report

This 77-year-old lady was admitted for partial mechanical gastric outlet obstruction. She had a subtotal gastrectomy, vagotomy, and B II gastrojejunostomy performed ten years previously, which had worked well until 18 months prior to surgery. In the months prior to admission she had developed two gastric bezoars which had been successfully treated with enzymatic digestion. However, her intake had been progressively restricted to pureed food and liquids; she was eating poorly and had lost approximately ten pounds. Upper G.I. showed partial gastric outlet obstruction and a dilated afferent loop; endoscopic biopsy showed a benign stricture. Past medical history was significant for mild hypertension adequately controlled with Hygroton, one tablet daily. She also had mild osteoporosis for which she was taking Os-cal t.i.d. and Premarin, 1 tablet daily three weeks per month. In addition, she was taking ferrous sulfate 300 mg. daily, multivitamins daily and folic acid daily. Other medications included celunase daily for digestion of recurrent gastric bezoars. The review of systems was negative for CNS, cardiovascular, pulmonary, renal, hepatic, or adrenal disease. Physical exam disclosed a vigorous, alert, thin, elderly lady. B.p. 118/60, p. 90, weight 96 lbs., height 59 inches. HEENT: negative. Lungs: clear. Cardiac: I/IV systolic ejection murmur in the aortic area. Abdomen: old transverse epigastric incision, soft, non-tender, no organomegaly, no masses. Lab. Hb. 11.2 MCV 88 Plts 470,000 PT: 11.9 Urinalysis: spec grav. 1.006 Ph 6 Prot. neg. Gluc neg. Ketone Neg. Bili Neg. Microscopic WBC/HPF 25-50 RBC/HPF 0-2 No crystals seen No casts SMA 12: TP 5.6 gm% CA 8.2 gm% P 2.7 mg% Chol 198 mg% G 135 mg% BUN 13% Uric Acid 2.6 mg% Creat 1.2 mg% Tot. Bili .3 mg% Alk Phos 83 unt LDH 117 unt SCOT 18 unt. Serum electrolytes: Na 133 mEq/ml K

3.3 mEq/ml Cl 99 mEq/ml CO<sub>2</sub> 30 mEq/ml. Serum gastrin 69. Holander test neg.

On 7-21-78 she underwent an uneventful resection of the old gastrojejunostomy with establishment of a new B II anastomosis. Pathology disclosed a benign inflammatory stricture at the old gastrojejunal anastomosis. Operative time was three hours 25 min. Intraoperatively she received 2,000 cc crystalloid (D5RL 1250 cc, N.S. 250 cc, D5.2N.S. 500 cc) and one unit whole blood, remaining hemodynamically stable throughout the procedure.

She also did well initially. The following morning, 7/22, she was alert, oriented, and able to ambulate. B.p. 140/60 p. 90 afebrile, weight 96<sup>3</sup>/<sub>4</sub> lbs., only minimally above pre-op. Urine output 30-40 cc/hr. Lab. Hb. 11.0 Na/K 125/4.5 Total intake for that second day was 2700 cc (2500 cc maintenance D5.2N.S. + 30 mEq KC1/1 plus 200 cc nasogastric replacement D5.45N.S. + 10 KCL/1). Output was 1750 cc.

The following morning, 7-23, she also looked well. Weight 94 lbs, urine output 80-90 cc/hr. The same i.v. solution was continued. However by that evening, 7/23, she had become confused and disoriented. Serum electrolytes from 10:00 p.m. Na/K 108/3.7 Cl/CO<sub>2</sub> 80/28. She was afebrile and vital signs were stable. During the 24 hours prior to detection of the hyponatremia she received 2400 cc i.v. fluid; the urine output was 2435 cc., and she showed no signs of overhydration. At this time she was given 600 cc normal saline over 4 hours and electrolytes were rechecked 7/24 4:00 am Na/K 112/3.7. This represented a slight improvement in the hyponatremia, and at this time she was given 200 cc of 3 normal saline followed by 200 cc of normal saline and again electrolytes were rechecked in four hours. 7/24 8:00 am Na/K 113/3.5. CL/CO<sub>2</sub> 83/28. Not only did hypertonic saline now fail to correct the hyponatremia but her clinical status had deteriorated significantly. She was markedly disoriented, talking incoherently, and had developed a left hemiparesis with rigidity of the left upper and lower extremities, hyperactive reflexes, and inability to deviate her eyes to the left. Pupils reacted sluggishly to light. However fundi showed no sign of papilledema, Babinski was negative. A spinal tap was then performed, which was negative. An EEG showed a diffuse dysrhythmia mixed with patterns of sleep. Hemodynamics remained stable, b.p. 160/80 p. 78 respiratory rate 18 weight, as pre-op, 96 lbs. Urine output 125 cc/hr.

At this time then the results of the urine and serum osmolality returned. 7/24 am. urine osm 453 mOsm/kg., urine Na/K 138/54 mEq/ml. At this same time the serum osmolality was markedly less:

\*Rochester, Minnesota.

†Minneapolis, Minnesota.



Serum osm. 225 mOsm/kg serum Na/K 113/3.5 mEq/ml. The elevated urine osmolality in the face of a markedly reduced serum osmolality indicated significant excess free water retention. In addition, there was nearly quantitative excretion of infused saline. This then was diagnostic of the syndrome of inappropriate secretion of antidiuretic hormone: hyponatremia with corresponding hypo-osmolality of the serum together with the production of a hypertonic urine and renal sodium excretion in a patient with normal renal and adrenal function and not volume depleted.

In addition the results of the serum Mg. indicated significant hypomagnesemia. 7/24 serum Mg 1.3 (Normal 1.8-2.5).

With fluid restriction (50cc/hr), infusion of hypertonic saline (2N.S.), replenishment of serum magnesium (3 gm MgSO<sub>4</sub>), and high dose corticosteroid therapy by the following morning, 7/25, the patient was lucid with complete resolution of the neurological symptoms.

She subsequently had an uneventful postop course. The C.T. scan, 7/26, was negative for focal findings. With continued fluid restriction the serum osmolality and serum sodium concentrations rose to normal levels over the next few days, and the urine osmolality progressively fell. Serum Na on 7/25 was 120, serum osmolality 224. Urine Na 36, urine osmolality 181. 7/27 serum Na 130, serum osmolality 263, urine Na 21, urine Osmolality 179. 7/31 serum Na 141.

**Syndrome of Inappropriate Secretion of ADH**

A brief review of the syndromes of inappropriate secretion of ADH and hypomagnesemia follows.

ADH is synthesized in the hypothalamus and stored in the posterior pituitary. When secreted it causes increased permeability of the renal collecting ducts to water resulting in passive reabsorption of water into the renal medulla, thence into the systemic circulation with the production of a concentrated urine.<sup>41</sup>

A second biological action seen with high doses is peripheral and splanchnic vasoconstriction, for which the hormone was originally named Vasopressin.<sup>26</sup>

Normally there are three stimuli for ADH release:

1. increased tonicity of fluid bathing hypothalamic osmoreceptors. The resultant secretion of ADH causes increased absorption of free water by the kidney with lowering of plasma osmolality. Hypotonicity causes the opposite response inhibiting ADH release and increasing renal free water clearance thus raising serum osmolality. This is the major physiologic action of ADH.

2. A second release system involves the low pressure volume receptors in the left atrium. These stimulate the pituitary through the Vagus nerve. A drop in left atrial pressure results in increased secretion of ADH and thus increased renal free water retention.

3. Thirdly, baroreceptors located along the major vessels mediate ADH release. A drop in arterial pressure stimulates ADH secretion by the pituitary. Thus hypertonicity and/or hypovolemia are the major stimuli for ADH release.<sup>26</sup>

In addition to these stimuli, however, there are a variety of others which result in potentially excessive ADH secretion. Central nervous system pathology, pulmonary disease of a variety of types, somatic and visceral pain, and certain drugs.<sup>18</sup> Moreover certain tumors, particularly small cell carcinoma of the lung produce ectopic ADH.<sup>9</sup> If large amounts of ADH are released the inhibitory effect of hypotonicity on ADH secretion can be overridden. In such situations there is excessive absorption of renal free water even in the presence of serum hyponatremia with resultant water intoxication. This situation has been termed the syndrome of inappropriate secretion of ADH, first recognized by Bartter and Schwartz in relation to bronchogenic carcinoma, 1957, and subsequently noted in relation to many other conditions,<sup>3</sup> particularly central nervous system dysfunction and pulmonary pathology (Table). Recently, elevated ADH levels have been documented by radioimmunoassay in this syndrome.<sup>40</sup>

**TABLE**  
**Causes of the Syndrome of Inappropriate Secretion of Antidiuretic Hormone**

<b>I Central Nervous System Pathology</b>
a. CVA
b. Meningitis
c. Brain tumor
d. Psychosis
e. Head trauma
<b>II Pulmonary Pathology</b>
a. Empyema
b. Pneumothorax
c. Pneumonia
d. Tuberculosis
<b>III Ectopic ADH Production, particularly Oat Cell Carcinoma of the Lung.</b>
<b>IV Pain</b>
<b>V Drugs</b>
a. Chlorpropamide
b. Demerol
c. Barbiturates
<b>VI Myxedema</b>

In many instances, particularly when the serum sodium concentration does not fall below 120 mEq per L., the patient may have no complaints and the syndrome does not become clinically apparent. The development of symptoms is related both to the degree of drop in the serum Na and to the rate of decline. With significant hyponatremia the earliest disturbance is often nausea and sometimes vomiting. The patient usually also becomes irritable and may show striking personality changes, becoming uncooperative, confused, or hostile. When the serum sodium concentration is reduced to less than 110 mEq per L., neurological abnormalities occur with loss of reflexes, muscular weakness, bulbar or pseudobulbar palsy,



positive Babinski's sign, stupor and seizures. At this stage the hypotonicity of body fluids poses a serious threat to survival.<sup>3</sup>

When the diagnosis is suspected in a patient with hyponatremia without evidence of volume depletion, it is confirmed by demonstration of a low serum osmolality with an inappropriately high urine osmolality in absence of renal and adrenal disease: this is indicative of excessive retention of free water in the face of serum hypoosmolality.

Under these circumstances, the primary treatment is not saline infusion, but fluid restriction. Since the primary defect is excessive ADH secretion with excess free water retention, fluid restriction will prevent a continued depression of the serum sodium and concomitant water intoxication. If large volumes of saline are infused, the sodium will only be excreted quantitatively in the urine as the body excretes sodium to remain normovolemic. Indeed failure of the serum sodium concentration to rise is a diagnostic feature of the syndrome of inappropriate secretion of ADH. Fluid restriction not only prevents further depression of the serum sodium concentration but also causes the retention of urine sodium for the maintenance of intravascular volume, as fluid intake falls below fluid output.<sup>33</sup> This often is sufficient treatment. If the patient has severe water intoxication, one may in addition infuse hypertonic saline and give high dose corticosteroids to inhibit ADH release. Hypertonic saline in small volumes will allow for the excretion of excess free water in the process of the renal clearance of the sodium load. Steroids increase sodium retention and may inhibit ADH release.

In this case the patient showed no signs of either fluid overload or volume depletion in the face of severe hyponatremia. Moreover she had no coexistent renal, adrenal, hepatic, or cardiac disease to cause her to excrete Na and retain free water. She thus fulfills well the criteria for the syndrome of inappropriate secretion of antidiuretic hormone: hyponatremia with corresponding hypo-osmolality of the serum in the presence of renal sodium excretion and the production of a concentrated urine. As is typical of this syndrome infused saline is promptly excreted without correcting the hyponatremia. Fluid restriction promptly reverses the precipitous fall in the serum sodium concentration.

The trigger for the start of this syndrome here is not entirely certain. It is our view that hypomagnesemia

was the precipitating factor.

### Hypomagnesemia

Hypomagnesemia is a syndrome which has not received wide-spread clinical attention. Most commonly Mg deficiency occurs in patients with chronically poor nutrition,<sup>36</sup> e.g. patients with chronic partial bowel obstruction, malabsorption, alcoholism, and post small intestinal by-pass for obesity, or those NPO for prolonged periods post operatively. A second group includes patients with chronic renal magnesium wasting states such as prolonged diuretic therapy with Lasix or high output renal failure.<sup>2</sup>

The metabolism of magnesium has been much neglected in current basic science research and little is known of its action by the body. Mg. is the second most plentiful cation within cellular fluids, and an important activator of many enzyme systems, especially Na/K ATPase dependent membrane pumps. Serum Mg level is maintained within narrow limits (1.8-2.5). It is absorbed from the upper small bowel and excess Mg is excreted in the urine. It takes several months on a Mg free diet to become hypomagnesemic.<sup>16</sup>

Rats on a Mg free diet after several weeks startle easily and develop seizures with stimulation. Much the same picture is seen in man of hyperexcitability and lowered seizure threshold.<sup>5</sup>

In addition, one may see an associated hypocalcemic tetany which is unresponsive to calcium infusion.<sup>2</sup> Also cardiac arrhythmias: supraventricular or ventricular,<sup>37</sup> occur. Most commonly one sees a seizure disorder, as occurred in this patient.

### Summary

The syndrome of inappropriate secretion of antidiuretic hormone has not been reported in association with symptomatic hypomagnesemia and may indeed just be an incidental finding in this case. However, no other trigger for the inappropriate ADH is readily apparent here and the association may result in physiologic synergism. This case stresses the importance of the determination whether the patient with hyponatremia needs sodium repletion or volume restriction. In addition, it emphasizes the importance of determining magnesium levels as well as electrolytes in patients with chronically poor nutrition who develop neurologic abnormalities.

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- 3-16. Will be found on page 414.





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# Minnesota Coalition on Health Care Costs

RICHARD J. FREY, M.D.\*

The Minnesota Coalition on Health Care Costs has moved from a recommendation to a reality. The Coalition developed from the Minnesota Medical Association sponsored Health Care Costs Commission which issued a series of recommendations in May of 1979. Among its 41 recommendations, the original Commission recommended that a non-profit Coalition be formed to implement the Commission's strategies for improving the cost-effectiveness of health services in Minnesota.

The newly formed Board of the Coalition includes representatives of hospitals, physicians, government, health insurance companies, businesses, educational institutions and the general public. The Board has met twice in the past few months and has taken significant steps to define an action program.

The Coalition hired a full-time staff. The Board selected James B. Kenney, Ph.D. as Executive Director of the Coalition. Jim is an experienced administrator who directed school health programs in the Minneapolis Public Schools the past nine years. Prior to his school system experience, he was a faculty member in the Medical School at the University of Minnesota. He has worked extensively with private and public health programs and professionals.

At the most recent Coalition Board Meeting, we defined the following major goals as the basis for our organization's program action:

I. To review, revise where appropriate, and support implementation of the concepts and recommendations embodied in the final report of the Minnesota Commission on Health Care Costs, 1979.

II. To monitor health service cost trends in Minnesota in order to improve choices and decisions regarding the purchase of health services.

III. To develop additional initiatives directed at improving cost containment methods and environments in the state and nation.

We expect to implement the first goal by using a task force approach. We have organized subgroups of the original recommendations of the Cost Commission for

further definition and implementation by one of three respective task forces. *The Task Force on Incentives* will develop incentives directed at encouraging health care providers and institutions to improve the cost-effectiveness of health services. A *Professional Education Task Force* will develop specific strategies for educating providers on needs for cost consciousness and means to reduce costs. We expect such educational activity will also target health science students as an integral part of their training. A third group of recommendations will be the concern of the *Health Promotion Task Force*. This task force will seek implementation of a statewide effort involving public and private resources to improve prevention, health education, and health promotion initiatives. Such a task force was specifically recommended in the original Commission report.

Funding support for the Coalition in the first three years will be provided by a combination of grants from private foundations and the business community. The Northwest Area Foundation has shown leadership in providing the initial start-up grant for the Coalition. The Hennepin County Medical Foundation has also provided some funding support for early Coalition activities.

The following are newly elected officers of the Coalition:

R. J. Frey, M.D., Chairman — Previously, Chairman, Minnesota Commission on Health Care Costs.

James S. Hetland, Vice-Chairman — Senior Vice President, First National Bank of Minneapolis.

Lars Carlson, Secretary — Director of Public Affairs, H. B. Fuller, St. Paul.

James R. Pratt, Treasurer — Vice President, General Mills, Minneapolis.

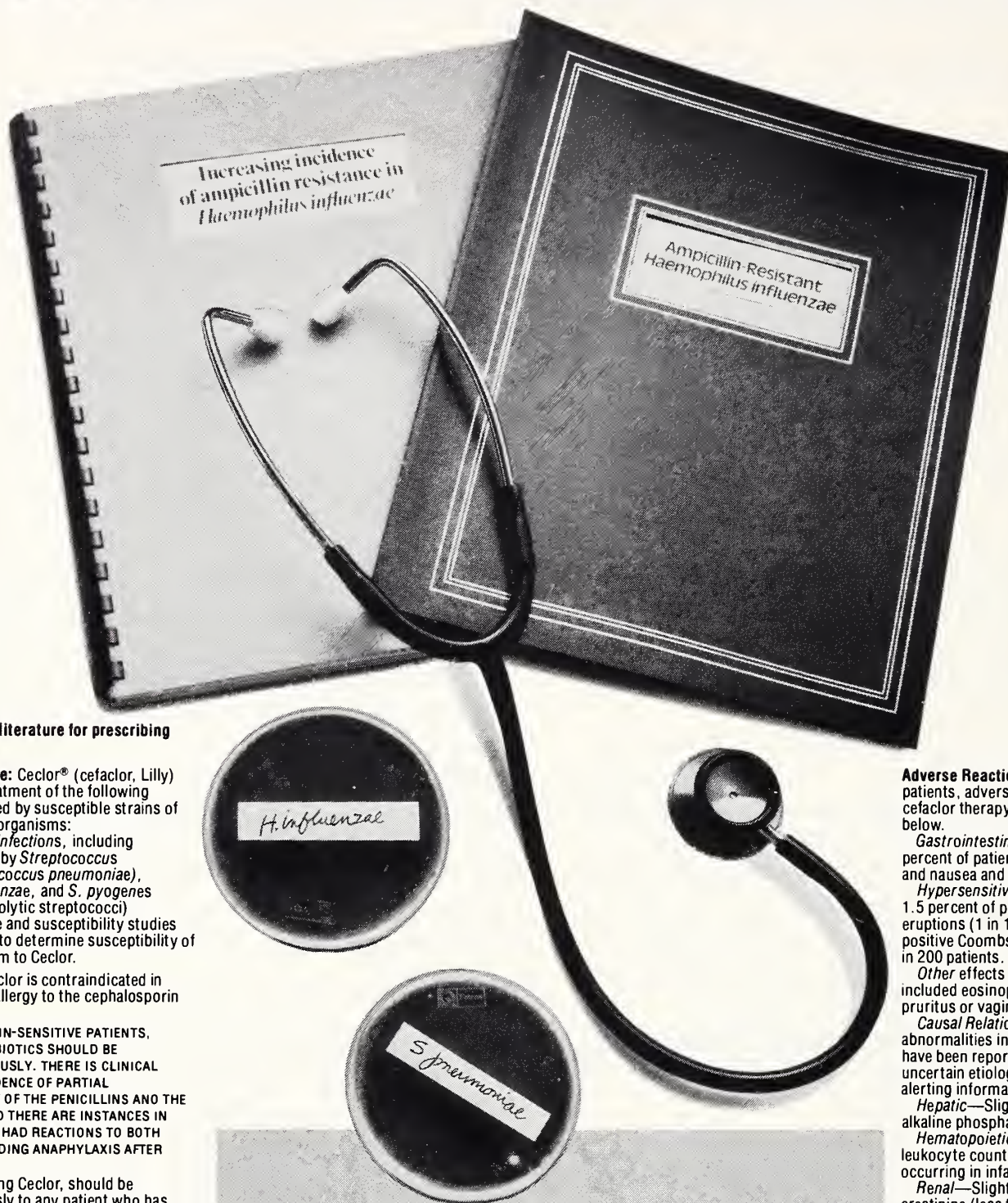
We will keep you informed of further Coalition activity through periodic reports in MINNESOTA MEDICINE. In the meantime, if you have any comments or suggestions that you think would be helpful to the work of the Coalition, please contact Jim Kenney or

me at: Minnesota Coalition on Health Care Costs  
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\*Previous Chairman, Minnesota Commission on Health Care Costs.



# An added complication... in the treatment of bacterial bronchitis\*



**Brief Summary.**  
Consult the package literature for prescribing information.

**Indications and Usage:** Ceclor® (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

*Lower respiratory infections*, including pneumonia caused by *Streptococcus pneumoniae* (*Diplococcus pneumoniae*), *Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci). Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

**Contraindication:** Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

**Warnings:** IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS TO BOTH DRUG CLASSES (INCLUDING ANAPHYLAXIS AFTER PARENTERAL USE).

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

**Precautions:** If an allergic reaction to cefaclor occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of cefaclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such a condition, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

**Usage in Pregnancy—**Although no teratogenic or antifertility effects were seen in reproduction studies in mice and rats receiving up to 12 times the maximum human dose or in ferrets given three times the maximum human dose, the safety of this drug for use in human pregnancy has not been established. The benefits of the drug in pregnant women should be weighed against a possible risk to the fetus.

**Usage in Infancy—**Safety of this product for use in infants less than one month of age has not been established.

**Some ampicillin-resistant strains of *Haemophilus influenzae*—a recognized complication of bacterial bronchitis\*—are sensitive to treatment with Ceclor.<sup>1-5</sup>**

In clinical trials, patients with bacterial bronchitis due to susceptible strains of *Streptococcus pneumoniae*, *H. influenzae*, *S. pyogenes* (group A beta-hemolytic streptococci), or multiple organisms achieved a satisfactory clinical response with Ceclor.<sup>7</sup>

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*Other* effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

*Causal Relationship Uncertain—*Transitory abnormalities in clinical laboratory tests results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

*Hepatic—*Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

*Hematopoietic—*Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

*Renal—*Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[070379R]

\*Many authorities attribute acute infectious exacerbation of chronic bronchitis to either *S. pneumoniae* or *H. influenzae*.<sup>8</sup>

**Note:** Ceclor® (cefaclor) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

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Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285. Eli Lilly Industries, Inc. Carolina, Puerto Rico 00630

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# Letters to the Editor

## HMOs

Dear Editor:

I just read your editorial in the February, 1980 MINNESOTA MEDICINE.\* I enjoyed your analysis of the merits and short-comings of HMOs. I had not been aware of all the unique population characteristics that made Minneapolis/St. Paul fertile fields for HMO organizations.

My purpose for writing this letter, however, was not solely to comment on HMOs. I would like to refer you to several sentences taken from the third paragraph of the editorial, under the section labeled "Physicians' Attitudes", you state "Physicians feel differently: After all, they didn't go into medicine to be controlled by an organization or to be subjected to its disciplines. They are *men* of knowledge and independence, capable of deciding what's best for themselves and their patients." I was wondering why you didn't include any women of knowledge and independence in your discussion.

I realize that these statements include figures of speech and are not meant to discriminate against women physicians. However, MINNESOTA MEDICINE is the official publication of the Minnesota Medical Association, and there are a good number of women physicians in the state of Minnesota. I would hope that statements coming through MINNESOTA MEDICINE would reflect equally and pertain equally to all physicians.

Lorraine A. Kretchman, M.D.  
Edina, Minnesota

\*Page 77.

## Unsuccessful Pregnancy

Dear Editor:

I read with interest the article entitled "Unsuccessful Pregnancy. Protocol for Management of Unsuccessful Pregnancy" by Drs. Hodgson and Ditmanson that appeared in the February 1980 issue of *Minnesota Medicine*.\* I learned a great deal about the scientific management of unsuccessful pregnancy. However, I was extremely shocked that no discussion of the need for emotional and psychological support attending an unsuccessful pregnancy was considered. I am sure this was an oversight, however, I feel it is a serious one.

Ralph A. Franciosi, M.D.†  
Minneapolis, Minnesota

\*Page 134.

†Director Minnesota Sudden Infant Death Program.

Dear Editor:

In the second paragraph of the paper entitled "Unsuccessful Pregnancy — Protocol for Management of Unsuccessful Pregnancy" (Minn. Med. 63, 134-138) we have listed as the third complication of the usual expectant management, the "psychological trauma and inconvenience of having to carry a dead or malformed fetus for an indefinite length of time." The fact that expectant rather than aggressive therapy is still used in this part of the country prompted the article in the first place.

Therefore we regret any impression left with any reader that the need for emotional and psychological support of such a patient is not great.

Saint Paul-Ramsey Hospital has an excellent group of counselors particularly well experienced in this field. Each patient in this report was individually counselled in depth and closely followed throughout her entire ordeal and given all the emotional and moral support possible. I certainly agree with Dr. Franciosi that the psychological ramifications of this subject are many and could easily furnish material for several additional papers.

I wish to thank Dr. Franciosi for his emphasis of this point.

Jane E. Hodgson, M.D.  
Saint Paul, Minnesota



## Nicotinic Acid

Dear Editors:

I recently had occasion to question why nicotinic acid sometimes causes a superficial vasodilatation (flushing) and pruritic response after it had been ingested. According to Goodman and Gilman,<sup>1</sup> "the most prominent pharmacodynamic action of nicotinic acid is a direct effect on blood vessels." The action is mainly that of a superficial vasodilatation associated with itching and burning. According to Scheinberg,<sup>2</sup> there is no corresponding increase in cerebral blood flow. To the best of my knowledge, this action of nicotinic acid is thought to be chemical in nature, but I have always wondered why it is inconsistent in its action for producing this vasodilatory response. Sometimes the reaction occurs and sometimes it is absent.

I recently had a patient who was eating yogurt three times daily, once at each meal. I started her on niacin 100 mg. four times daily and for two days, she had severe reactions to each dose of niacin. She requested that I stop the niacin because of her discomfort, but rather I discontinued the yogurt. Immediately, the patient had no further reaction of either flushing or pruritis when taking the same dose of niacin.

It would appear that niacin was probably pharmacologically blocking some vasoconstrictor effect produced by some other mechanism. In other words, vasodilatation itself probably is a passive reaction in which vasomotor tone is decreased rather than a direct active response. If blood vessels are not constricted, there may be no significant vasodilatation.

In order to explain the reaction which I observed in this particular patient, I had to assume that the yogurt was in some way producing vasoconstriction. Then, when the patient took niacin, she experienced vasodilatation by niacin blocking the vasoconstrictive action. When the patient did not eat yogurt, she did not have relative vasoconstriction; consequently, she did not experience any significant relative vasodilatation after taking niacin.

To further speculate on a possible mechanism for the vasoconstriction that must have been present following this patient's eating yogurt, if the patient had been allergic to the yogurt, it would seem reasonable that she would develop a degree of inflammation of her intestinal wall. This would permit the absorption of a number of vasoconstrictor amines as well as endotoxin through a less competent bowel wall. Endotoxin is well known for being a strong direct vasoconstrictor of blood vessels.

Subsequently, the patient did try skimmed milk and again she had a severe reaction to niacin. This would suggest that she indeed was having some type reaction to milk products generally.

Since my experience with this particular patient, I have had many occasions to test this hypothesis on a number of patients. There is no question that niacin definitely causes flushing in individuals when specific foods are consumed, although these foods may vary from patient to patient. Each individual has his own specific foods that are more prone to cause a flushing reaction after taking niacin. I do feel that it is not always reliable, but it certainly happens often enough to suggest that different foods might be allergenic to any one patient. The method I have been using involves taking niacin 100 mg. one hour before meals. If the patient has a flushing reaction during that hour, I assume that they probably are reacting to some food that they have eaten at a previous meal. On the other hand, if the reaction begins within five to ten minutes after their beginning to eat, the reaction probably is the result of consuming a particular allergenic food at the time that they are eating. I have been using this technique to help assist in determining what foods might be allergenic to any specific individual while beginning a hypoallergenic food elimination diet. In other words, I am using niacin as a diagnostic tool rather than a therapeutic medication.

I do not feel that niacin is invariably accurate in determining specific allergenic foods. Possibly this is because other substances that are absorbed into the body may also cause a reactivity to niacin. Specifically I have been using elimination diets in treatment of multiple



## LETTERS TO THE EDITOR

sclerosis, assuming that absorption of endotoxin from the intestinal tract may have a detrimental effect on the inflammatory lesions of multiple sclerosis in the central nervous system. This could be through a mechanism of a Shwartzman reaction.<sup>3</sup> It is well known that infections generally have a detrimental effect on multiple sclerosis. This mechanism could be an explanation for progression of multiple sclerosis in the absence of obvious infection.

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Waterloo, Iowa

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### Formation of the Upper Midwest Regional Endoscopy Society (UMRES)

This organization has as its purpose the education of physicians regarding gastrointestinal endoscopy as well as quality assurance in the continued use and performance of these procedures. It is a non-profit organization whose charter has been filed with the State of Minnesota in 1979. Membership is open to physicians in the State of Minnesota and adjacent states who have interest, training, and proficiency in gastrointestinal endoscopy. Specific requirements for membership are outlined in the By-Laws of the organization. At the initial meeting at which time the constitution and By-Laws were adopted, the following officers and Board of Directors were elected.

President: Alphonso A. Belsito, M.D., St. Paul, Minnesota.

Secretary: Arnold P. Kaplan, M.D., Minneapolis, Minnesota.

Other officers of the Board of Directors are: Jack A. Vennes, M.D., Minneapolis VA Hospital, Rollie M. Hughes, M.D., Mayo Clinic, and John B. King, M.D., Mayo Clinic.

Physicians wishing to obtain more specific information regarding the organization are invited to inquire at the office of,

Arnold P. Kaplan, M.D., Secretary, UMRES  
2545 Chicago Avenue  
Minneapolis, MN 55404

A spring meeting and program are being planned.





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# Special Article

## Depression in a Medical Setting

JOHN DRUCKER, M.D.;\* JOHN HEEFNER, M.D.;† and RUSSELL WILDER, M.D.‡

### Dr. John Heefner:

Historically depression as a human condition can be traced to antiquity. The early Egyptians had no word for it but recognized and treated it relying heavily upon the power of suggestion. Old Testament references provide glimpses of depression. Hippocrates was responsible for early written records of depression then called melancholia. Not until the 19th century did the word "depression" enter common usage. This followed Kraepelin's description of the manic depressive syndrome. Most historical accounts have been consistent in describing depressed individuals as gloomy, morose, hopeless, inactive, and preoccupied with a view of reality incongruent with that of others.

Depression is a common malady.<sup>1</sup> It is regarded by many as the most common psychiatric illness. Estimates suggest it may affect up to 10% of Americans at any one time. Most go untreated. Each year from four to 8 million Americans are treated for the disorder. Some 250,000 are hospitalized.

The illness has widespread implications. It contributes to untold personal and social problems including alcoholism and other drug addictions, school dropouts, marriage and other personal relationship difficulties, job discontent, etc. It is a disease having considerable impact on the economy costing the country between 1.3 and four billion dollars annually. Suicide, the fatal outcome of many depressions, claims over 20,000 lives each year in this country. The actual number is probably higher.

Several problems exist in establishing the diagnosis of depression and thereby obstructing the correct diagnosis. One problem is a semantic one relating to definition. Depression may be described as a syndrome, such as congestive heart failure, and not a specific diagnosis. It may be considered a feeling state like sadness unaccompanied by the other classic signs and symptoms. Society may find depression a socially

unacceptable problem as evidenced by the ready condemnation and rejection of Thomas Eagleton during the 1972 election year when it was disclosed he had had a successfully treated depressive illness. Professionally it may not be acceptable. Many may remember the double suicides several years ago of a university medical school professor and his wife. The teacher's colleagues had recognized the depression but had been reticent to mention it, each hoping someone else would. Oftentimes the illness isn't recognized by the patient as well as the physician when it occurs as a constellation of somatic complaints or as a part of another illness such as cancer or functional bowel disease.

Symptoms of depression represent a broad spectrum.<sup>2</sup> On one end is the ordinary sadness or blueness all experience at times. These feelings are usually short-lived and not persistent or pervasive. Next on the spectrum occurs the normal grief reaction experienced secondary to losses usually through death or separation. These symptoms are usually short-lived and respond well to appropriate support. Following grief reaction comes the "reactive" depression or "neurotic" depression. Last on the spectrum is the "endogenous" or "psychotic" depression. From the symptom of sadness to the syndrome of psychotic depression depressive symptoms move from transient duration to prolonged, and everyday functioning moves from near normal to almost totally disabled. While mood symptoms are common to all variations of the illness, somatic and cognitive complaints increase as one moves towards more serious disease. Treatment varies, as well, in that for less serious illness support is often enough, whereas with more severe disorders combined psychotherapy and drug management may be indicated.

The best approach to the diagnosis of a depressive disorder is a careful and detailed clinical history. This requires working knowledge of the signs and symptoms of depression and a patient capable of reporting an accurate history. Occasionally supporting data must be obtained from the depressed individual's family and/or friends. The clinical manifestations of depressive illness are multiple and often present in varying combination. Diagnostic aids are available to

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assist in making the diagnosis of depressive illness. The depression scale, scale number two, on the Minnesota Multiphasic Personality Inventory (MMPI) is useful in supporting the diagnosis when the scale is appropriately elevated. The Hamilton Depression Scale is a 23-item scale which is a widely used examiner rated instrument for the clinical assessment of depressive states.<sup>3</sup> The Zung Self-Rating Depression Scale is a 20-item questionnaire completed by the patient which is useful for evaluating depressive symptoms and for following response to treatment.<sup>4,5</sup> The Research Diagnostic Criteria for making the diagnosis of a major depressive disorder will be presented later. The characteristic signs and symptoms to which one should be alerted when seeing individuals with possible depressive illness will be discussed under the headings emotional, cognitive, and vegetative.<sup>6</sup> Such a breakdown is somewhat artificial as there usually is a combination of manifestations.

First, the mood of most depressed individuals is one of sadness or dejection. However, in a significant number this is lacking, and other features predominate. This is especially true in the so-called "masked" depression which may go undetected or misdiagnosed. Many terms are used by individuals to describe their feelings. Common are such expressions as sadness, blueness, down in the dumps, hopelessness, emptiness, don't care, irritability, anxiousness, worried, etc. In order to appreciate this one must acquire some understanding of an individual's pre-morbid mood and behavior. Not infrequently individuals employ somatic equivalents in describing their feelings. These include such things as "a lump in my throat," a "weight on my chest", "a broken heart", or "an emptiness in my stomach."

Along with depressed mood individuals complain of loss of interest in pleasurable activities. There may be a decrease or loss of emotional attachments particularly to family members and to friends. Frequent crying spells or the feeling one wants to cry are not uncommon. There may be a diminution in response to humor. Anger, often internally directed, occurs and contributes to lowered self-esteem. Anxiety, not infrequently a prominent feature in depression, especially in that of the agitated variety, may be misleading. Prescribing minor tranquilizers makes the underlying depressive symptomatology worse. Often more drug is prescribed because of lack of improvement, and a vicious cycle ensues.

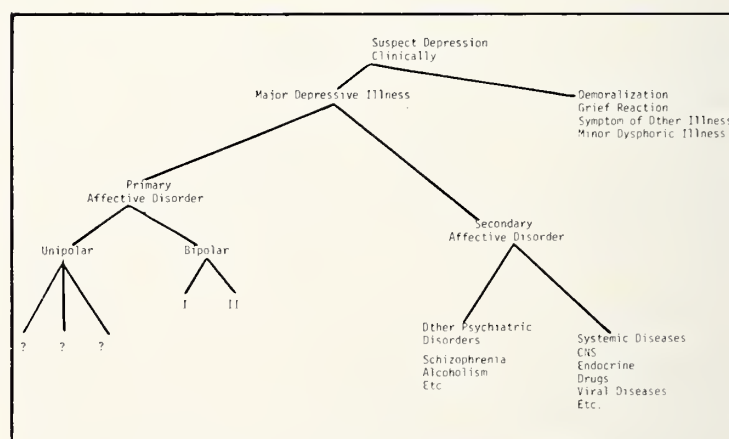
Various cognitive manifestations occur in depressive disorders. There may be complaint of inability to remember which, when formally tested, is not found.

Difficulty with concentration in depressed patients may account for some of the apparent trouble remembering about which the individual expresses concern. Thinking processes, in general, slow down with decreased quality, quantity, and spontaneity of thought. These may make the differential diagnosis of depression and early dementia difficult.

Difficulty in making decisions can be immobilizing and may interfere with the ordinary tasks of daily life. Self-blame with feelings of inappropriate guilt are often observed and may assume paranoid proportions especially in involutional melancholia.

Distorted attitudes towards and preoccupation with oneself are common. Self-esteem is negative, and an individual who is feeling badly about himself is not easily reassured. Expectations of events and of others are viewed pessimistically and may be forerunners of suicide. Body image may become distorted assuming a delusional quality, particularly, in involutional melancholia.

Somatic manifestations of depression may predominate masking the basic problem. Choice of symptoms may be symbolic and related to self-image and self-concept. Appetite change is common varying in degree from anorexia to increased appetite. Concomitant with appetite changes goes weight loss or gain. In general weight loss in depression should not exceed one pound per week or ten pounds per year depending upon duration of illness. Gastrointestinal complaints are common, including a tendency towards constipation, dry mouth, and indigestion. Also seen are individuals with diarrhea, various abdominal pains, unusual taste, and unexplained gastrointestinal effects from various medications. Sleep patterns are altered and may take one of several varieties. Insomnia is most common, but hypersomnia may also occur. Psychomotor retardation with a general slowing of most bodily and mental processes characterizes the majority of depressions. In the agitated individual



Figure



movements are also altered and tend to be excessive but purposeless, repetitive, and stereotyped.

Non-specific symptoms such as loss of energy, fatigability, and tiredness, often accompanying nonspecific organ system complaints such as shortness of breath, palpitations, headache, etc., make the distinction from organic medical illness difficult. Sexual dysfunction may occur in several forms such as diminished libido in both men and women. Secondary functional impotency, common in men, and painful intercourse may be present. Studies suggest these dysfunctions may be related to decreased androgens present in chronic depression as well as to decreased catecholamine and increased cortisol found in chronic stress.<sup>7</sup> Pain complaints are frequent and tend to be diffuse and non-specific. Headaches, of the tension or musculoskeletal variety, occur and tend to be chronic. Neck and back pain, particularly low back pain, are seen and often unresponsive to usually prescribed analgesics.

The following case reports illustrate three different types of depressive illness. They also highlight many of the features of depression described. They come from a group of 100 consultations with major diagnoses of depressive disorders seen during a six month period in 1977 by the Psychological Medicine Section at the Minneapolis Veterans Administration Hospital.

### Case Histories

#### Prolonged Grief Reaction

A 50-year old man was admitted to the Medicine Service for evaluation of epigastric distress. The workup was negative, and the patient was referred to Psychological Medicine for consideration of the functional nature of his symptoms.

The patient described himself as a hard-working and somewhat stoic man who had always been restless but more so in the past month. It was during this time that his stomach began bothering him.

Further history revealed his wife had been killed in an automobile accident six months before and that his son had been killed in a similar accident 12 months previous to that. He took only a week off work following his wife's death.

He related an increased sense of restlessness, decrease in appetite, social withdrawal, increased drinking, crying spells when alone, and a feeling of imposing on family and friends. Examination revealed him to be anxious and somewhat downcast.

Brief supportive treatment was accomplished in the out-patient clinic. There was prompt resolution of his symptoms.

#### Endogenous Depression

A 50-year old man was admitted to the Medicine Service for evaluation of abdominal pain. He was referred to us because of anxiety and questionable functional overlay to his symptoms.

Questioning revealed the patient to be a tense man who had been quite successful despite numberable obstacles. At the time of his hospitalization, however, things had been going quite well. Nonetheless, he had been experiencing increased irritability,

decreased libido, insomnia, anorexia, pessimism about his future, lack of interest in ballgames and friends, and concern that "chemicals" were out of balance. His affect was depressed.

He was treated with 150 mg of Doxepin daily and followed in the out-patient clinic. Four months following hospitalization he was symptom-free with no abdominal complaints and no depressive symptoms.

#### Reactive Depression

A 30-year old man was followed in the Medicine Clinic for chest and abdominal pains of vague character. He was referred to us for evaluation of his emotional state.

History revealed the patient had been unexpectedly and recently fired from a job he very much liked. Loss of the job prompted a move back to Minneapolis where the patient and his wife were living with the wife's parents. He had been unsuccessful in getting a job and was financially impoverished. Physical symptoms began shortly after they moved to Minneapolis. These were associated with insomnia, marked decrease in energy, trouble concentrating, constant ruminations about his lost job, irritability, and negative self-concepts. He appeared appropriately despondent.

Doxepin, 150 mg at bedtime, was recommended along with vocational counseling. He gradually improved with resolution of the external conflicts.

### New Concepts in Depression, Proposed Etiologies

#### Dr. John Drucker:

Several methods of classifying depression have been traditionally applied. While clinically useful, none are based on good scientific studies of depressed patients. During the past 15-20 years new investigations have produced knowledge necessitating revision of previous nosology. These have covered five major areas: more careful descriptions of signs and symptoms of depressive illness, genetic and family studies of affective illness, longitudinal studies of outcome, laboratory investigations, and studies of response to medication treatment. These studies have resulted in a new classification of affective disorders which is likely to be accepted when the Diagnostic and Statistical Manual-III is published. This classification is schematically summarized in the Figure and is almost identical to the Research Diagnostic Criteria for affective disorders proposed by Spitzer, Endicott, and Robins<sup>8</sup> (Table).

A patient who appears clinically depressed must be evaluated for the presence of chronic demoralization resulting from poor psychosocial adjustment, a grief reaction, depression as a symptom of physical illness or a psychiatric disorder, and minor dysphoric illness, a syndrome which does not meet the full criteria for major depressive illness. The diagnosis of major depressive illness can be made if the patient meets the criteria listed in the Table.

These criteria have been developed for research purposes to exclude "false positives" (that is, patients



without true depressive illness) from research designs. Rigid application to clinical practice would too frequently lead to undertreatment of patients. However, they do offer a reasonable guideline for diagnosis. In clinical practice the diagnosis of depressive illness depends on the intensity, duration, and quality of psychopathological features.

Secondary depression must meet exactly the same phenomenological criteria as primary depression. The only difference is whether there is pre-existing physical or non-affective psychiatric illness. The secondary classification does not imply the depression is a result of the pre-existing condition but merely associated with it. Probably the majority of major depressive illnesses seen on medical in-patient wards are secondary depressions associated with a documented systemic illness. Those depressions with physical complaints, but without systemic disease, are considered primary depressions. They have been referred to as "atypical" or "masked" depressions because the patient minimizes or denies his dysphoric

mood focusing on the somatic complaint. Such patients may complain of anxiety. Treatment for presumed physical illness does not relieve the complaint, but treatment with anti-depressants relieves the physical symptomatology. In these patients it is important for the physician to probe for marital, family, job, financial problems, etc. which may be contributory and require psychologic counseling.

Recent family studies<sup>9,10</sup> have validated the division of the affective disorders into unipolar and bipolar groups, the former consisting of depression without mania and the latter including episodes of both mania and depression. First degree relatives of patients with manic depressive illness have eight to ten times greater likelihood of developing this illness than the general population. Relatives of unipolar depressives have two to five times the risk of the general population for developing unipolar depression. Approximately 10% of bipolar patients' relatives and 5% of unipolar patients' relatives are affected. Bipolar illness occurs at an earlier mean age (33.6 years) than unipolar depression (mean age 48.6 years). Twin studies support a genetic component to affective illness as monozygotic twins are 75% concordant for manic depressive illness while dizygotic are only 20% concordant. Clinical, pharmacologic, and neurophysiologic studies have lent support to the bipolar-unipolar division.

Biochemical investigations have begun to modify the simplistic concept of elevated brain norepinephrine in mania and lowered norepinephrine in depression known as the "catecholamine hypothesis" of affective disorders.<sup>11</sup> Recent theories have synthesized the findings of differential patient response to anti-depressants, in vitro drug activities on biogenic amines, and the elucidation of the roles of serotonin and 3 methoxy-4hydroxyphenethyleneglycol (MHPG). The latter is a urinary marker for brain norepinephrine metabolism. It is now believed there are two biochemically distinct types of depression in patients with a biological component to their illness.<sup>12</sup> Patients with type A depression have low levels of urinary MHPG when clinically depressed, reflecting a deficit in the level of brain norepinephrine. This group responds to imipramine but not to amitriptyline. A trial of amphetamine in this group will lead to increase in mood, whereas patients with type B do not experience elevated mood with amphetamines. MHPG in the type A group will return to normal following successful treatment with imipramine. Patients with type B depressions have normal or slightly elevated urinary MHPG levels when depressed which remain stable or

**TABLE**  
**Research Diagnostic Criterion**  
**for Major Depressive Illness**

- A through D required for the episode of illness being considered.**
- A. Dysphoric mood characterized by symptoms such as the following: Depressed, sad, blue, hopeless, down in the dumps, empty, "don't care", irritable, anxious, worried. The dysphoric mood must be prominent and relatively persistent but not necessarily the most dominant symptom.**
- B. At least five of the following symptoms are required for definite and four for probable (for past episodes, because of memory difficulty, the criteria are four and three symptoms).**
- 1. Poor appetite or weight loss or increased appetite or weight gain (change of 1 lb a week or 10 lbs a year when not dieting).**
  - 2. Sleep difficulty or sleeping too much.**
  - 3. Loss of energy, fatigability, or tiredness.**
  - 4. Psychomotor agitation or retardation (but not mere subjective feeling of restlessness or being slowed down).**
  - 5. Loss of interest or pleasure in usual activities, or decrease in sexual drive (do not include if limited to a period when delusional or hallucinating).**
  - 6. Feeling of self-reproach or excessive or inappropriate guilt (either may be delusional).**
  - 7. Complaints or evidence of diminished ability to think or concentrate, such as slow thinking, or mixed-up thoughts (do not include if associated with obvious thought disorder).**
  - 8. Recurrent thoughts of death or suicide, including thoughts of wishing to be dead.**
- C. Dysphoric features of illness lasting at least one week. Definite if lasted more than two weeks, probable if one to two weeks.**
- D. Sought help from someone or was referred for help during the dysphoric period, took medication, or had impaired functioning socially, with family, at home, or at work.**



return to normal following successful treatment with amitriptyline. They do not respond to treatment with imipramine.

Although these studies have been done on patients with primary affective disorders, it is quite possible similar differences exist in patients with secondary affective disorders. A recent publication<sup>13</sup> demonstrates that symptom patterns are similar in primary and secondary depressions. Unfortunately, there is no way to clinically differentiate type A from type B depressions at this time. However, one practical clinical implication can be drawn from the above findings. A patient who has failed to respond to anti-depressant treatment with one drug (e.g. imipramine) after an adequate trial should be tried on at least one other (e.g. amitriptyline) before deciding that the depression is refractory to drug treatment.

### Treatment Approaches

#### Dr. Russell Wilder:

Depressed patients most often seen in daily practices are suffering from reactive depressions. Much information is required about these patients before initiating treatment. It is essential to know if the patient has had previous episodes of depression and how they were treated. Likewise has a psychotic depression ever occurred?

It is important to know how impulsive the patient is, what kinds of things he has done in the past on the spur of the moment. A careful and methodical housewife began talking about death and fears of driving to her doctor's office. She described being afraid she might run into a bridge or an embankment "accidentally". During discussions it developed she was driving her husband's shiny new well-kept automobile. Damaging it just didn't fit her style, and both realized she was in no danger.

Is the patient alcoholic? The suicide rate in people with chemical dependency is high. Therefore, a drinking, depressed patient is an increased risk.

What has the patient thought about death? If he denies having thought about it, he is probably the only person who never has had such thoughts. Everyone has at one time or another thought for most persons it is something that happens only to other people. Almost everyone has at one time or another thought about suicide. If a patient says he never has, one might ask, "how come?" If an individual says he has thought about suicide and he thinks about it often, inquiry should be directed as to how he would do it. Does he have a rope in the barn? Does he have a piece of hose to attach to the tailpipe of his car? Is he saving pills? Is he

thinking about bridges? Does he keep a loaded revolver in his drawer? Such inquiry is urgently important. Most patients appreciate an opportunity to talk about their suicide thoughts and impulses and find it very helpful. If the patient says "yes" to the inquiry about a loaded gun and appears a serious risk, he ought to be admitted to a protective facility rather than an open medical ward. If the patient has been saving pills or has a gun in his desk drawer he should be encouraged to give them to a friend or the physician or the minister or to anybody whom he trusts. Even in ideal situations suicide is not totally preventable, but the patient needs to know his physician is concerned, interested, and trying to help.

It is important for the physician to appreciate that techniques of treating and managing a depressed patient are different than for the patient with a physical complaint.

The tendency to approach problem solving by the use of a highly reasoning process is standard procedure for most conditions. It is to be avoided when working with a depressed patient. Openness and honesty are required, and instead of the accustomed professional relationship, a supporting one which reflects the patient's current feelings is required.

It is well, also, to be mindful of the contagious quality of the depression which, if not recognized, can soon complicate the physician's effectiveness.

Avoid being too cheerful and too familiar. Likewise, overoptimism and reassurance is contraindicated as the patient very likely won't believe you. In his own eyes he is not worth saving and, in addition, cannot live up to his own expectations.

At all cost avoid joking or trying to be humorous. If the patient smiles occasionally smile along with him but refrain from any light remarks which, in all probability, will be misinterpreted as his being made fun of.

The usual stylized routine of working with a patient should be discarded. Instead an effort should be directed toward partially identifying with and relating to him as comfortably as possible. This is a difficult task which requires care and persistence.

For some patients deep in gloom and certain nothing is even going to get better, the task is not to be too kind or sympathetic, overly warm and too friendly. There are times when direct but gentle confrontation is the approach. On occasions the kindest thing to do is to say "You know, you're going to have to get off your duff."

It is important and essential to encourage the patient to be busy. If he has hobbies, every effort should be



directed toward his working on them. While in hospital, a program of occupational therapy may initiate the restoration of self-esteem. Gardening, walking, bicycling — any outdoor activity — are excellent therapies against depression. Keep encouraging the patient to keep busy with even mundane activities such as polishing silver, painting the bathroom, or sanding and refinishing old furniture in the house. Doing so may irritate the patient to the point of becoming angry. If so, his response will be therapeutic as externally directed anger is a sign of improvement.

If the patient is not suicidal, psychotic or troubled by a bipolar condition, the general physician or internist, if interested, can care for him without referral. Depressed patients should be seen, particularly if on medications, at least once a week. If marital difficulties are suspected, husband and wife should be seen together.

As mentioned previously, the patient, when improving, will begin to manifest irritation and anger directed primarily at the physician. This is to be expected and should occur during the second or third week of treatment. Even though objective signs of improvement are noted, the patient may deny this and complain nothing has been done for him. This is part of the process of improvement to be expected and should not deter the physician from continuing his support and encouragement.

ECT is not indicated for most of the patients we've been discussing. This treatment modality may be useful for severely depressed patients who have been referred to a psychiatric unit for treatment. Monoamine oxidase inhibitors should not be used today. They're too risky. Sedatives have no place in the treatment of most depressions. This is particularly true of Librium and Valium since the underlying depressive state tends to worsen with their use. Amphetamines and Ritalin, while they've been previously advocated, are not useful and are intensely habit forming. Mellaril, because of unpleasant side effects, generally is to be avoided unless there is considerable agitation.

Finally, we come to a useful and controversial group of drugs undoubtedly helpful for many patients with depressive illnesses. At the physician's disposal is a fairly broad spectrum of tricyclic antidepressants starting with doxepin and continuing through amitriptyline, imipramine, norpramine, etc., all of which

have trade names. They vary in the amount of sedative and energizing effects produced. Imipramine is probably more energizing and a bit less sedating than amitriptyline. Doxepin is quite heavily sedating which may be of advantage for patients who are anxious and agitated. Sometimes overstimulation occurs with the tricyclics which may suggest having missed an underlying psychotic process or thought disorder. Patients with such response may begin to complain of crazy thoughts or become quite agitated. Triavil, a combination of amitriptyline and perphenazine, is useful for the depressed patient who fits into this category.

There are the usual side effects from these drugs. The atropine-like effects are relatively mild but can be minimized through careful dosage management in patients with glaucoma and in those with severe prostatic hypertrophy. In patients with recent myocardial infarctions or with evidence of rhythm disturbances caution is indicated with their use. If a tricyclic is required in a patient who has had a recent myocardial infarction, doxepin is probably the safest choice.

Most of the tricyclic antidepressants in common usage have an average daily maintenance dose of approximately 150 mg. Fortunately most individuals can take the drugs as a single nighttime dose. This tends to minimize the side effects and promotes a greater compliance in drug taking. It is well to remember it takes anywhere from ten days to three weeks before the anti-depressive effects of the drug are noted. If, after that time, improvement is not evidenced, increased dosage may be indicated before changing to another agent. Medication should not be discontinued abruptly following successful treatment of depression. The dosage should be reduced gradually by one tablet at a time over a period of several weeks. In some instances one needs to "feel your way down" to determine if the depression has cleared or whether residuals remain requiring attention. A number of patients are very slow to respond. However, one of the encouraging things about most depressions is they eventually terminate spontaneously whatever is done. This is the case if physician and patient can wait. Meanwhile, even if chemical therapy has been ineffective, physician support will undoubtedly be beneficial.

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5-17. Will be found on page 393.



# Rheumatology Corner

## Corticosteroid Drug Therapy in Rheumatoid Arthritis

CONRAD BUTWINICK, M.D.\*

THE DEMONSTRATION of the powerful anti-inflammatory effects of cortisol by Hench initially suggested the long awaited wonder drug for arthritics had been found. However, it quickly became apparent that the use of steroids often resulted in a trade of one disease for another, at times with a most serious outcome.

The use of steroid drugs in the treatment of rheumatoid arthritis has evolved as a series of basic principles that, while not universally agreed upon, in general have found acceptance among those treating arthritics. The anti-inflammatory response and prompt alleviation of acute arthritic symptoms may be substantial. It is generally agreed, however, that steroids do not alter the overall course of the rheumatoid state and the potential toxicity is added to the burden of the underlying arthritis. Obviously before steroids are considered, the use of a conservative program including rest, physiotherapy, and high dose salicylates or other non-steroidal anti-inflammatory medications should be tried. Additionally, a remission inducing program utilizing medications, such as gold or penicillamine, may be initiated before or in conjunction with the use of steroids.

When major arthritic activity involves only a few joints, the use of intra-articular steroids may be a better solution than the use of systemic steroids. Often triamcinolone hexacetonide (Aristospan) is used for intra-articular use. Its large molecular size impedes absorption through the synovial membrane, both minimizing systemic toxicity and resulting in a prolonged therapeutic effect that may last several weeks or more. Typical dosages used for intra-articular injection include as much as 1.5 cc. into large joints, such as hips and knees, with 0.5 to 1.0 cc. doses into smaller joints, such as shoulders, elbows, and ankles. Wrists generally are injected with 0.5 cc., and small hand and foot joints with less than that. Concern over the deleterious effects within the joint from repeated steroid injections exists, especially as it relates to

accelerated cartilage injury and impaired cartilage healing, but usually the risk of unchecked arthritis exceeds that of the steroid injection. Our experience thus far suggests it to be a clinically appropriate therapeutic tool.

Systemic steroids in a rheumatoid patient should be given daily, preferably in a once in the morning dosage. Alternate day steroids generally mean alternate day arthritis and, while one may be minimizing some of the steroid toxicity, the purpose for which the steroid is given is not being met.

Prednisone is generally the steroid of choice as an oral agent. It is inexpensive and comes in 1 mg., 5 mg., 10 mg., and 20 mg. tablets which allow great flexibility especially during steroid withdrawal when often very tiny reductions are necessary to avoid flaring the underlying disease. As little as 3 to 5 mg. of Prednisone daily may achieve substantial relief of arthritic symptoms while keeping the total steroid burden to a minimum. I try to keep patients on less than 10 mg. of Prednisone daily and always look to minimize the dosage of steroid even by as little as 1 mg.

An adrenally suppressed patient is in jeopardy when exposed to stress, such as acute illness, surgery, or emotional trauma, and may need temporary supplemental coverage.

Steroid withdrawal should be accomplished keeping the rule of 25 % in mind. If tolerated, a reduction every five to 10 days of up to 25% of the dose is recommended. This seems to work well, especially at higher dosage levels, but, as implied above, once one is down to a dosage of 10 mg. or less, the reduction may have to be accomplished at a much slower pace.

An excellent review of the use of corticosteroids in rheumatoid disease may be found in *Rheumatic Disease* edited by Warren Katz and published in 1977 by J. P. Lippencott Company.

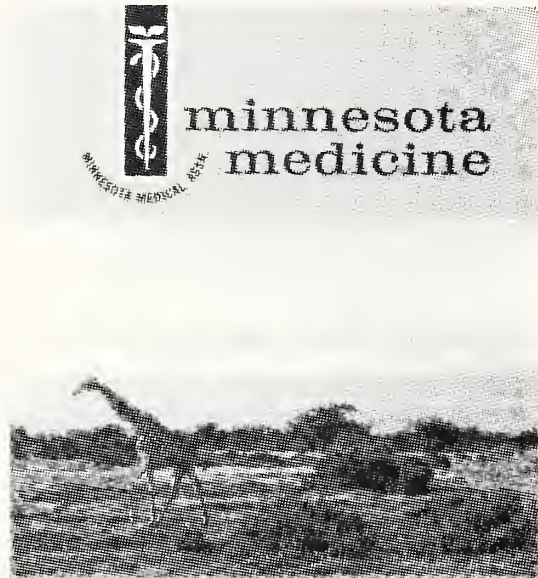
\*Assistant Clinical Professor of Medicine, University of Minnesota, Minneapolis. Private practice, St. Paul.



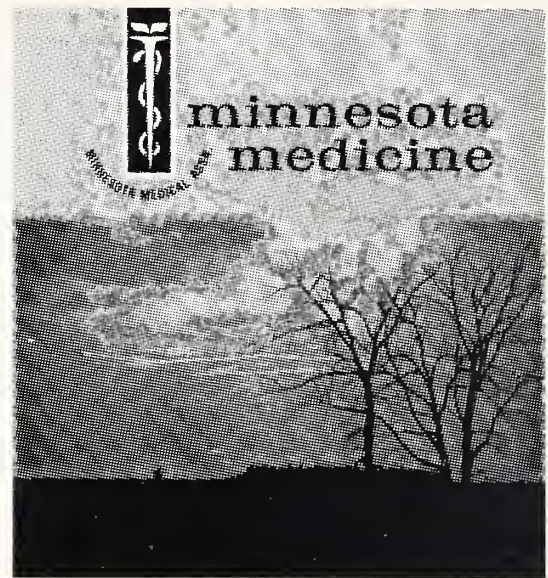
# MINNESOTA MEDICINE's Best of the Year

Each Spring the Board of Editors announces its choices for the best scientific/original article and best cover for the previous year. The winners for 1979 are:

## Best Covers



"Two Tall Ones in East Africa", December, 1979 issue of MINNESOTA MEDICINE by Oliver H. Peterson, M.D., Obstetrician/Gynecologist practicing in Minneapolis.



"Early Spring in Minnesota", March, 1979 issue of MINNESOTA MEDICINE by Carl M. Kjellstrand, M.D., Chief of Nephrology Section at the University of Minnesota Health-Sciences Center, Minneapolis.

## Best Articles

### 1,000 Renal Transplants at the University of Minnesota 1963-1977

BRUCE G. SOMMER, M.D.; DAVID E. R. SUTHERLAND, M.D.; CARL M. KJELLSTRAND, M.D.; RICHARD J. HOWARD, M.D.; S. MICHAEL MAUER, M.D.; RICHARD L. SIMMONS, M.D.; and JOHN S. NAJARIAN, M.D.

Between June 7, 1963, and September 1, 1977, 1,000 renal transplants were performed at the University of Minnesota. On January 1, 1978, 70 per cent of the recipients were alive and 64 per cent had functioning grafts. The results of transplantation at a single institution are analyzed according to recipient risk factors and period of transplantation.

RENAL TRANSPLANTATION at the University of Minnesota Hospitals was first undertaken on June 7, 1963 by Dr. Richard L. Varco. On September 1, 1977, the 1000th transplant was performed at the same center by Dr. John S. Najarian. During the intervening 14½ years renal transplantation has become an accepted and effective method of treatment for end stage renal failure.<sup>1-4</sup>

From 1963 to 1967, Dr. William Kelly and many other physicians collaborated in the pioneer venture of renal transplantation at the University Hospital.<sup>5</sup> In 1967 Dr. John S. Najarian assumed responsibility for the transplant service, and one year later, Dr. Carl M. Kjellstrand, a nephrologist, and Dr. Richard L. Simmons, a surgeon, joined the program. These three individuals formed the nucleus of a transplant team that has made the University of Minnesota one of the largest transplant centers in the world. The University of Minnesota experience with 1,000 transplants in 866 recipients and virtual 100 per cent followup is the basis for this report.

#### Patient Population and Methods

Between June 7, 1963, and September 1, 1977, 566 renal allografts from related donors and 434 renal allografts from cadaver donors were transplanted to 866 patients (499 males and 367 females). There were 853 first, 128 second, 15 third and 4 fourth transplants. Thirteen patients (11 nondiabetic and 2 diabetic) had their first transplants elsewhere. One patient had a second transplant elsewhere, but a first and third transplant at the University of Minnesota. The ages of

the recipients at the time of transplantation ranged from six weeks to 72 years.

Approximately 3 per cent of all patients referred to the University of Minnesota during this time span for treatment of end stage renal failure have not been transplanted because of: (a) the presence of malignancy, (b) extreme age, (c) multiple severe complications of diabetes mellitus and other systemic diseases, (d) the presence of cytotoxic antibodies to potential donors, or (e) the patients' preference for chronic hemodialysis.

Prior to 1968, patients were selected for transplantation on the basis of factors believed to place them in a good risk category. Since 1968 liberal criteria have been used, and many patients categorized as "high risk" have received kidney transplants.<sup>6-8</sup> During the last seven years an increasing proportion of patients with diabetes mellitus,<sup>9-10</sup> collagen diseases,<sup>11</sup> enzyme deficiencies,<sup>12</sup> vascular disease and urinary tract anomalies<sup>13</sup> have been transplanted. The commitment

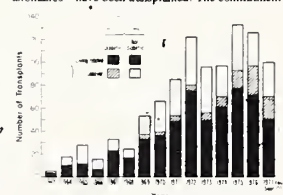


Fig. 1—Renal transplants at the University of Minnesota by year, donor source and presence or absence of diabetes, June 7, 1963 to September 1, 1977.

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### History

Thomas E. Keys

Medical Librarian, Historian, Scholar, and Author—Extraordinarius

JACK D. KEY, M.S., M.A.

THOMAS KEYS graduated from Beloit College, Beloit, Wisconsin, in 1931, with the degree of Bachelor of Arts and received his M.A. degree from the Graduate Library School of the University of Chicago in 1934. He was library assistant at the Newberry Library in Chicago in 1931 and 1932. He attended the University of Chicago as a Carnegie Fellow in the Graduate Library School in the fall of 1932 and held a graduate assistantship in 1933.

Keys came to Rochester, Minnesota, in 1934, as assistant librarian of the Mayo Clinic. He was appointed reference librarian in 1935, a post he held until 1942, when he was granted a leave of absence to become librarian in charge of rare books of the Army Medical Library in Cleveland, Ohio. He discharged the duties of this post with distinction and was awarded the Army Commendation Ribbon by the Surgeon General of the Army. He was promoted through the grades from first lieutenant to lieutenant colonel.

Returning to the Mayo Clinic as Librarian in 1946, Keys continued in that capacity until April 1, 1970, when he became senior library consultant. He retired in December of 1972. He was named assistant professor of the history of medicine of the Mayo Graduate School of Medicine in 1957, was advanced to associate

professor in 1963, and became professor in 1969. He was a member of the Board of Regents of the National Library of Medicine from 1959 to 1962.

During his tenure as Mayo Clinic Librarian, the holdings of the Mayo Clinic Library were greatly expanded; during World War II, for instance, it was recognized in Washington D.C. and elsewhere that the Mayo Clinic's collection of Russian periodical medical literature was the largest in the United States. The impressive acquisitions of rare books in the Mayo Clinic Library resulted almost entirely from the unceasing efforts of Dr. Keys in that endeavor.

Dr. Keys (Figure) revived and virtually single-handedly stimulated an abiding interest in medical history which has persisted at the Mayo Clinic and Mayo Foundation, and he is the author or co-author of a number of volumes on the history of medicine. On April 17, 1972, he was awarded the honorary degree of Doctor of Science by Beloit College, the citation reading in part: "Your lifelong commitment to excellence and innovation in your chosen career has helped in large part to create one of the world's greatest medical libraries and has won for you national distinction in the library profession."

Permanently active in professional association ac-

Figure—Thomas E. Keys



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"1,000 Renal Transplants at the University of Minnesota 1963-1977" by B. G. Sommer, M.D.; D. E. R. Sutherland, M.D.; C. M. Kjellstrand, M.D.; R. J. Howard, M.D.; S. M. Mauer, M.D.; R. L. Simmons, M.D. and J. S. Najarian, M.D., University of Minnesota Health Sciences Center, Departments of Surgery, Medicine and Pediatrics. Published in December, 1979 issue of MINNESOTA MEDICINE, page 861.

"Thomas E. Keys — Medical Librarian, Historian, Scholar, and Author—Extraordinarius" by Jack D. Key, M.S., M.A., Librarian, Mayo Clinic, Rochester, December issue, page 883.



# Indochinese Refugees

## Nutritional and Health Status In A Lao Refugee Camp

KAREN OLNESS, M.D.\* and ERIK TORJESEN†

The results of a pilot nutritional survey of 301 children in the Lao refugee camp at Nongkhai, Thailand are reported herein. General observations are made regarding the health status in the camp, its socio-cultural ramifications, and possible implications for health-care providers in Western countries where Lao refugees are resettled.

### Background

The health of Southeast Asian refugees in Minnesota has been the subject of several articles in recent issues of *Minnesota Medicine*.<sup>1-6</sup> In the past few months dozens of Minnesota physicians, nurses, and allied health professionals have gone personally to Southeast Asia to work in refugee camps.

This paper is written from the Lao refugee camp at Nongkhai, Thailand, where the authors represent the Minnesota International Health Volunteers (MIHV), a service-teaching-research project that intends to provide a continuity of health services through a rotation of volunteers for as long as the camp needs them. The project is supported by MIHV contributors, by the American Refugee Committee (ARC) of Minneapolis, and by the International Rescue Committee (IRC). Currently, the MIHV team consists of two pediatricians, two nurses, and two medical students.

Nongkhai is located in northeastern Thailand, across the Mekong River from Vientiane, the capitol of Laos. The refugee camp has been here for five years, with a recent population of about 30 to 40 thousand, most of whom are ethnic Lao. Despite a substantial movement of refugees leaving for resettlement and new escapees arriving from Laos, the camp is relatively stable for this region. Shortly after this report was written, a fire destroyed much of the camp and drove 20,000 refugees from their shacks. Reconstruction started immediately.

Basic rice supplies and fish sauce purchased by the United Nations are provided to legitimate refugees in the camp. Catholic Relief Services provide food for hospitalized patients as well as some supplementary foods for persons who do not qualify for the rice ration and for certain categories of women and children. Some supplementary food is provided by Food for the

Hungry, but the majority of meat, eggs, milk, fruit, and vegetables must be purchased by refugees from local markets. If they cannot afford such purchases, they must subsist on a diet of rice and fish sauce.

### Nutritional Survey

The clinical impression of nutritional status of children in the Nongkhai Camp is that there is little flagrant kwashiorkor or marasmus but a substantial "subclinical" malnutrition and stunting among pre-school and grade school children. Children who appeared to be about eight years old were actually 12 years and those who looked to be three years turned out to be six years. Weights and heights had not been routinely recorded in camp clinics in the past. We decided to undertake a pilot nutritional study of infants and children in order to have a more precise assessment of the nutritional status of the pediatric population.

### Method

The 301 children measured in this survey included 262 who consecutively presented themselves to the camp out-patient clinic for treatment during the last week of January 1980, and 39 pre-schoolers admitted to the camp day-care center who were measured on their second day in the center. Children surveyed ranged in age from two months to 12 years with the age breakdown as follows: 25 were 0-11 months, 38 were 1-2 years, 42 were 2-3 years, 40 were 3-4 years, 33 were 4-5 years, 41 were 5-6 years, 35 were 6-9 years, and 45 were 9-12 years. No children were included who presented with diarrhea and dehydration or obvious congenital defects which might affect growth adversely.

Height, weight, and length of time in the camp were determined for each child. Head circumference was measured in children under three years, arm circumference (Shakir strip method<sup>7-9</sup>) in children one to five years old, and triceps skin fold measurements in children six years old and above.

Heights, weights, and head circumferences were interpreted first in terms of the reference percentiles for American boys and girls constructed by the National Center for Health Statistics in collaboration with the Center for Disease Control. Weight for stature

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†"House Husband" of Dr. Olness.



comparisons were made in pre-pubertal girls and boys using American reference percentiles. Weights and heights were interpreted in terms of reference standards for Thai children prepared by the Thai Ministry of Health. Their graphs included a single curve for normal heights and weights and three progressively lower curves which represented first, second, and third degrees of malnutrition on the growth grids. These did not differentiate boys and girls.

Stigmata of clinical malnutrition were recorded for each child. These included such signs as lightened hair, chipmunk cheeks, decreased ear elasticity, edema, and a "flaking paint rash" on arms and legs.

### Results

For the group as a whole 38% of heights and 56% of weights were below American fifth percentile standards. Overall, 5% of children surveyed had clinical stigmata of malnutrition. For infants under 11 months, 15% of lengths and 38% of weights were below fifth percentile standards. For toddlers from ages one to two years 40% of heights and 59% of weights were below fifth percentile standards. These figures were quite uniform through older groups up to the nine to 12 year group which included 70% below fifth percentile references for weight and 54% below fifth percentile references for height. Twenty-four percent of this group were below fifth percentile references for weight for stature.

Of those Lao children falling below American fifth percentile standards for weight, 56% fell into the range of first degree malnutrition by Thai standards; 38% fell into the range of second degree malnutrition, and 6% fell into the range of third degree malnutrition.

Overall, 39% of boys between ages two months and 11½ (pre-pubertal) and 39% of girls between ages two months and 10 years (pre-pubertal) were below fifth percentile curves in weight for stature.

Of 39 pre-schoolers in the day care center, 46% were below American fifth percentile standards for weight, 31% were below fifth percentile standards for height, and 44% were below fifth percentile curves in weight for stature. Overall, 11% of pre-school children were above the fiftieth percentile in weight by American standards and 15% were above the fiftieth percentile in height by American standards. One child was above the 95% percentile in both height and weight.

According to Shakir strip arm circumference measurements, 35% of children between one and five years were malnourished. Of this group 61% were below the fifth percentile in weight for age measurements. Of all weights below the fifth per-

centile in children between ages one to five years, 49% were normal by Shakir arm circumference measurements.

Triceps skin fold measurements in children age six and above were found to be as follows:

13 mm —	5%
10-12 mm —	22%
8-10 mm —	14%
6-8 mm —	49%
3-5 mm —	10%

Forty-three percent of children under three years were below the fifth percentile for head circumference by American standards.

### Discussion

Results indicate a significant degree of malnutrition among Lao refugee children at the Nongkhai Camp. This manifests itself more in chronic stunting than in full blown syndromes of kwashiorkor or marasmus. Those children hospitalized for treatment of malnutrition fall into the clinical pattern of marasmus rather than kwashiorkor. This is interesting with respect to Whitehead's thesis<sup>10</sup> that kwashiorkor and marasmus cannot be explained simply on the basis of differences in diet protein or calorie intake but rather on the basis of different hormonal backgrounds perhaps established at an early stage in the child's life. In the case of marasmus, plasma cortisol levels are elevated, while they are low in children with kwashiorkor. The range of environmental stresses to which each child is exposed, according to Whitehead, determines whether or not kwashiorkor or marasmus emerges in a community. Marasmus seems to reflect greater degrees of environmental stress.

In the area of Vientiane, Laos (the area from which most refugees came to the Nongkhai Camp) 15 years ago most cases of severe malnutrition had the clinical appearance of kwashiorkor rather than marasmus. Environmental stresses of the refugee camp which affect Lao children there are undoubtedly different from those of the previous life style in Laos. One can speculate that increased crowding and increased exposure to infectious diseases as well as chronic anxiety in families may provoke hormonal responses and manifestations of malnutrition very different from those of the old placid life in Laos.

The possibility of diminished brain growth associated with malnutrition in the pre-school children should be of grave concern to the UN groups responsible for feeding these refugees as well as to third countries who will receive the refugees as new citizens. Although the issue of effects of early malnutrition on intellectual functions is far from



resolved, there are numerous controlled laboratory animal studies and uncontrolled human studies which suggest that some of the effects are permanent.

Of concern is the possibility that chronic malnutrition in children adversely affects optimal immune responses to viral, bacterial, and parasitic epidemics which abound.

The population of the day care center (39 children) was somewhat larger and better nourished than the overall group. This may reflect nepotism in Lao day care administration, i.e. the more highly educated Lao are involved in day care organization and arrange for their children or friends' children to be chosen. There is the possibility that parents lowered their children's ages in order to qualify for the ceiling age of five years.

The percentage of nine to 12 year olds under the fifth percentile was 70% for weight and 54% for height, while 74% of this group had normal weight for height ratios. This is consistent with stunting and may reflect poor nutrition preceding arrival in the refugee camp. However, overall, there was no correlation between duration of time in camp and extent of malnutrition. Refugees say that adequate food provision in the Vientiane area of Laos has been a problem for the past five years.

This survey found a poor correlation between the use of arm circumference measurements in children, ages one to five years, and malnutrition as reflected in weight for age discrepancies. The many false negatives are consistent with the findings of Margo and Cook<sup>11-12</sup> and suggest that this measurement is too inaccurate to be a worthwhile screening tool.

### **General Observations at the Nongkhai Refugee Camp**

Two dominant observations stand in sharp contrast. On the one hand, every western physician or nurse working here is likely to feel overwhelmed by the prevalence of disease and suffering. On the other hand, the resiliency and coping ability of the refugees is impressive. This was demonstrated by the reaction of 20,000 refugees rendered homeless by fire recently. Although the fire moved through the straw and bamboo shacks in 45 minutes, the escapees did not panic. Only one death occurred, a few hundred individuals suffered minor burns, and one patient was admitted with hyperventilation attributed to the stress. The next day the victims could be seen bending with dignity over the warm ashes to scrape for nails and wire to use in improvising temporary shelters. One must consider the reality that the refugee population is a rigorously selected one in which those who reached the decision

to flee their homeland and then survived the high attrition involved in getting to a refugee camp, tend to be the more indefatigable members of the society.

In the Nongkhai refugee camp which holds the second largest Lao community in the world (the first being Vientiane, the Lao capitol which once had a population around 70,000), all toilets are currently plugged, open sewers overflowing, and mosquitos breeding in many stagnant pools. Current epidemics include measles, falciparum malaria, infectious hepatitis, amoebic dysentery, chicken pox, mumps, and scabies. Not only children but many adults are admitted with measles and/or falciparum malaria, suggesting a previous lack of exposure. Tuberculosis is endemic.

Although the new regime of Laos has outlawed bad spirits entering hospitals, and patients no longer place knives in beds to stave off bad spirits, nearly every patient enters with fresh baci strings tied around his wrists. Ninety of one hundred consecutive patients whom we saw in the out-patient setting had taken a medicine purchased by themselves at a "pharmacy" in the camp. A favorite is chloramphenicol. One patient, age two, was admitted with hematemesis caused by a gastritis probably triggered by "many" aspirin given at home. Another, age sixty-three, was admitted with fansidar toxicity after, not only taking four fansidar tablets but also a fansidar injection within a period of four hours. A 17-year-old girl was admitted in septic shock 24 hours after a "nurse" put an unknown substance into her pregnant uterus. Patients with incomplete induced abortions are admitted every day; this was a rare occurrence in Laos 10 years ago.

In spite of increased crowding in the refugee camp, the life style is distinctly Lao, and one is impressed by the lack of preparedness for life in a third country. As huge groups depart by bus for the United States weekly, we wonder about the culture shock they may experience on arrival in our own state. Recently, volunteers have initiated orientation classes. These concentrate on such American necessities as using telephones, taking a bus, paying income taxes, prescriptions for drugs, making beds, cleaning bathrooms — all totally new concepts for the refugees.

### **Summary — Implications for Minnesota Health Care Providers**

1. Children from the Nongkhai refugee camp are likely to arrive in the United States with a significant degree of malnutrition. It would be useful if a protocol could be designed which would be used to follow a significant number of these malnourished children



over the next twenty years.

2. Refugees from the Nongkhai camp have lived under dreadful sanitation conditions and have been exposed to epidemics of measles, amoebiasis, infectious hepatitis, and falciparum malaria. Tuberculosis is endemic as are usual intestinal parasites and scabies. Rabid dogs have been identified frequently in the

camp. New arrivals in Minnesota from this camp may be incubating some of these diseases.

3. Refugees are accustomed to self medicating with both Lao and western medications and may have such armamentarium accompanying them.

4. Refugees, to this point, have not received any organized orientation for life in the United States.

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### Northwestern Pediatric Society Meeting

The annual meeting of the Northwestern Pediatric Society will be held on Friday, September 26, 1980, at the Chanhassen Dinner Theater, Chanhassen, MN.

Guest speaker for the occasion will be James G. Garrick, M.D., Director, Center for Sports Medicine, St. Francis Memorial Hospital, San Francisco, CA. Dr. Garrick's topic will be "Children and Sports: What Are the Problems?"

Abstracts of papers may be submitted to, or further information obtained from Stephen J. Boros, M.D., Secretary-Treasurer, Northwestern Pediatric Society, Children's Hospital, 345 North Smith Avenue, St. Paul, MN 55102.

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# Urban-Rural Suicide Differentials in Minnesota 1967-1973\*

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**Suicide rates for Minnesota Metropolitan and small urban counties increased while rural counties experienced a rate decrease. Suicide trends are identified for specific age-sex groups. If these trends continue, Minnesota's suicide rates may soon surpass the national average.**

**T**HE PURPOSE OF THIS REPORT is to describe recent Minnesota suicide trends in metropolitan, small urban, and rural Minnesota counties by age and sex. Descriptive hypotheses are tested by an analysis of suicide data made available to the authors by the National Center for Health Statistics.

Intentional self-destruction has long been used as an indicator for (1) disruption of interpersonal relations culminating in social isolation, (2) feelings of normlessness or anomie, and (3) mental anguish.<sup>1,2</sup> In the United States and other western countries, there are four or five times as many attempted suicides as successful suicides and many threats of suicide for every attempt.<sup>3</sup> Thus, although there were only 25,127 known suicides in the United States in 1973, these can be interpreted as an indicator of widespread maladjustment and pervasive mental anguish.

Rapid increases in geographic and social mobility are closely linked to the disruption of interpersonal relations. Thus, a rise in suicide rates follows increases in migration<sup>4,5</sup> and social mobility.<sup>6,7</sup> Most of the increase in suicide occurs among "newcomers", or those who have recently arrived at a new place or social position.

On the basis of these empirical generalizations, it is hypothesized that: (1) because of increasing opportunities for women and blacks during the time period 1967 through 1973 and the concomitant changes in social roles, increased mobility, and other factors, these groups should show a trend of increase in suicide rates; (2) these trends should be greatest in metropolitan counties because large urban areas are characterized by relatively greater influxes of people, employment relocation and social mobility.

The hypotheses are tested with suicide data from Minnesota counties for a seven year period, 1967-1973. Metropolitan counties are defined as the central city counties of Minnesota's four Standard Metropolitan Statistical Areas (SMSA) such as Ramsey County. Small urban counties are the 19 counties in Minnesota with one or more cities between 10,000 and 49,999 population. Rural counties are the 64 counties in the state without a city of 10,000 or more population. Suicide rates per 100,000 population were calculated from (1) population figures in the 1960 and 1970 United States Census, computer generated intercensal estimates for 1967-1969, and the United States Census Bureau estimates for 1971-1973 and (2) suicide death records for 1967-1973 supplied by the National Center for Health Statistics on standardized microdata computer tapes. Analysis is limited to the Minnesota white population due to the small number of blacks and the great variability of black suicide rates from 1967 to 1973.<sup>#</sup>

Utilizing data for each of the seven years, 1967-1973, statistical tests of significance were performed using analysis of variance and Duncan's multiple range test for variable log rates. Further, comparisons of trends by specific age groups were made by pooling rates for two three-year clusters, 1967-1969 and 1971-1973, and testing for statistical

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#The population of blacks is relatively small in Minnesota and this exaggerates the impact of even a single black suicide on percent change in black suicide rates. Thus, it is statistically unwise to make interpretations of rate changes for the black population. For example, Minnesota black male suicide rates range from a low of 5.8 per 100,000 in 1969 to a high of 42 per 100,000 in 1973, while the black female population experienced a decrease from 21.2 suicides per 100,000 population in 1967 to no reported suicides in 1971, 1972, and 1973. Further, meaningful urban-rural suicide rate comparisons for the Minnesota black population are impossible because so few blacks live in non-metropolitan areas. Many southern states have adequate numbers of blacks in both urban and rural areas to make statistically significant interpretations of rate changes. For example, Coombs and Barton have reported suicide trends in the Alabama black population 1967-1973<sup>8</sup>



significance of difference between clusters with a Z test.

Results

Suicide rates in Minnesota between 1967-1973 are less than those for the United States in the same period. For example, in 1973, overall suicide death rates in the United States were 12.0 per 100,000 as contrasted with Minnesota's rate of 10.4.

Individuals in each of the age-sex-area categories are variably subject to social circumstances, e.g. a metropolitan male of 27 normally lives and works in a different environment than a rural woman who is 50. Furthermore, residential environments subsume great variation in the social circumstances that affect individuals. Therefore, an analysis of suicide trends in metropolitan, small urban, and rural counties should reveal important variations in the frequency of suicide for different age and sex groups.

Table 1 demonstrates that male suicide rates in Minnesota are higher than female rates for all ages and the differential increases with age. Table 2 illustrates variation in suicide rates by area and sex: suicide rates are obviously highest in Minnesota's metropolitan counties, although rates for rural males are also relatively high.

A more detailed description of suicide trends in Minnesota is presented below.

Metropolitan Counties

In metropolitan areas of Minnesota, suicide rates between 1967-1973 rose 12% for the total population. Suicide rates for white males increased 10.6% compared to 11.1% for white females. An analysis of pooled suicide rates (a three year average) by age categories and sex for the white population of the metropolitan counties show five statistically significant ( $p \leq 0.05$ ) trends (Table 3). In both the male and female population, the younger age categories experienced the greatest increase in suicide rates. For males 0 to 24 years old, rates increased by 68% compared to a 73% increase for females. For the population 25-44, male suicide rates increased 20.8% and females experienced a 10.1% increase. In the age categories 45-64 and 65 and above for both sexes, suicide rates had no significant trend of increase. However, for males 45-64 there was a 12.5% decrease.

Focusing on sex differences in metropolitan suicide rates reveals that females have consistently lower rates than do males for all years between 1967 to 1973, and in all age categories. In 1973, male rates ranged from five times as high in the 65 and over age category to almost two times as high in the 25-44 age category.

TABLE 1

MINNESOTA POOLED SUICIDE RATES BY SEX AND AGE (1967-1973)

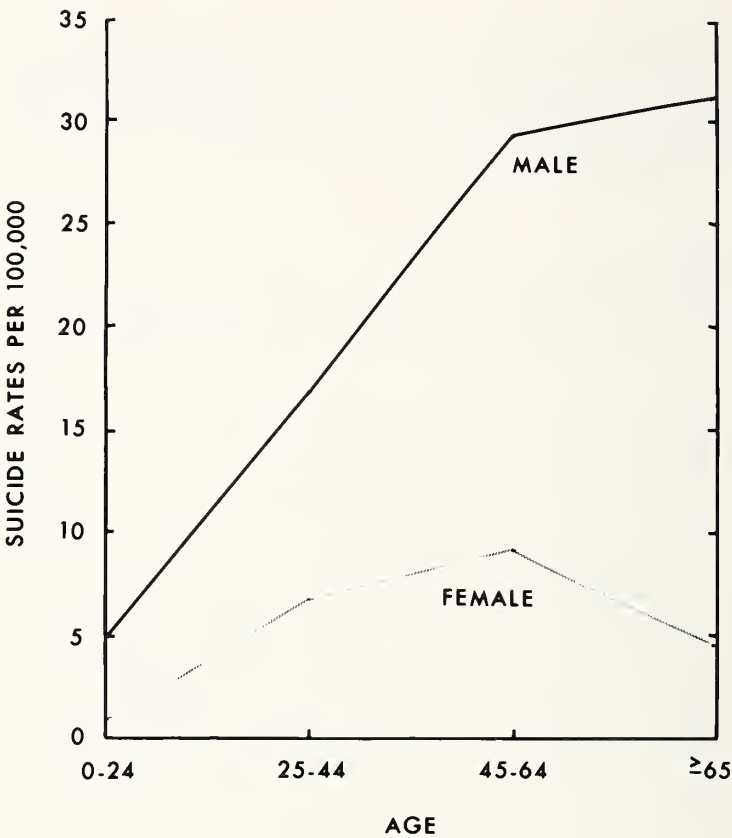
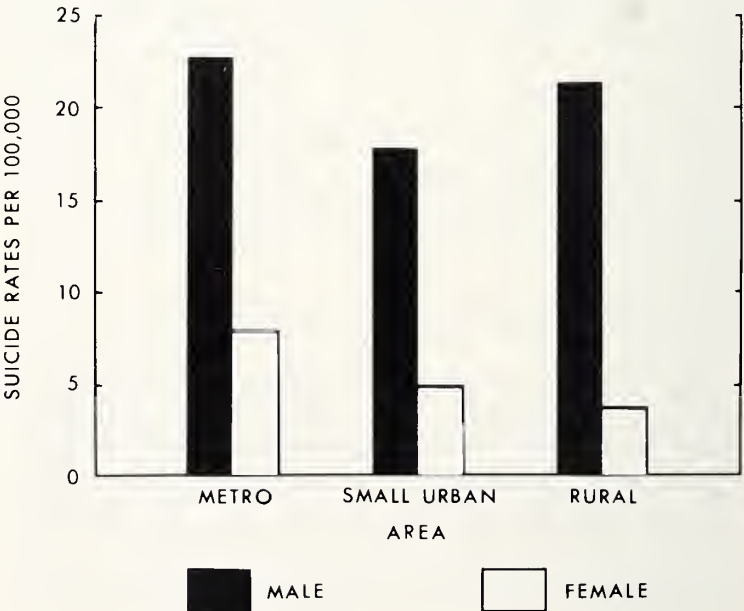


TABLE 2

MINNESOTA POOLED SUICIDE RATES BY AREA AND SEX (1967-1973)





*Small Urban Counties*

In the small urban counties, suicide rates for the total population increased 25.7% with males accounting for most of the increase. Analysis by age and sex reveals seven trends of statistical significance ( $p < 0.05$ ) (Table 3).

Males in the age categories 0-24, 25-44 and 45-64 experienced large increases in suicide rates during the 1967-73 period; 96.8% in the 0-24 age category, 46.8% for the 25-44, and 19% for the 45-64 category. This trend was not as evident among females. Suicide rates for women 0-24 years of age in small urban counties decreased and were lower than rates for any other area/sex/age group. However, there was an increase of 27.6% among females 25-44 years of age. In the 65 and above age group, both males and females experienced a decrease in suicide (-14.6% for males, -32.6% for females).

As was the case for the metropolitan areas, female suicide rates in small urban counties were much lower than male rates in all age groups. For the population 0-24 male rates were 15.3 times higher than female rates.

*Rural Counties*

In contrast with metropolitan and small urban areas, the total suicide rates in rural counties dropped by 9% between 1967-69 and 1971-73. Male rates overall decreased by 14.5% while female rates increased 3.6%. When the data are examined by age group, there emerge seven statistically significant trends ( $p < 0.05$ ) (Table 3). Rates increased slightly, but significantly, for both sexes in the 0-24 age category. In the 25-44 age category, male suicide rates decreased 6.4%, while female rates decreased by 62.7%. For the 45-64 age group, male rates decreased by 33.8%, while female rates increased by 86.7%. As in the other areas, all rates for females were much lower than for males.

**Discussion**

The hypothesis that females would experience an increase in suicide rates (1967-1973) was partially supported. Some groups were affected more than others: there were significant increases in rates for females 0-24 in metropolitan and rural areas; also for females age 25-44 in metropolitan and small urban areas; and for females age 45-64 in rural areas.

TABLE 3  
Suicide Rates by Age and Sex for the White Population  
Metropolitan,<sup>1</sup> Small Urban,<sup>2</sup> and Rural Counties,<sup>3</sup>  
in Minnesota 1967-69\* and 1971-73\*

	1967-69	1971-73	%Change	1967-69	1971-73	%Change	1967-69	1971-73	%Change
0-24									
Male	4.7	7.9	68.1†	3.1	6.1	96.8†	4.0	5.0	25.0†
Female	1.5	2.6	73.3†	0.6	0.4	-33.3†	0.6	0.9	50.0†
25-44									
Male	17.3	20.9	20.8†	13.9	20.4	46.8†	15.7	14.7	-6.4†
Female	9.9	10.9	10.1†	5.8	7.4	27.6†	5.1	1.9	-62.7†
45-64									
Male	33.7	29.5	-12.5†	20.5	24.4	19.0†	39.1	25.9	-33.8†
Female	11.9	12.0	0.8	7.4	8.3	12.2	4.5	8.4	86.7†
65+									
Male	32.0	33.7	0.5	27.3	23.3	-14.6†	32.5	33.5	3.1
Female	6.6	6.8	3.0	4.9	3.3	-32.6†	3.3	2.7	-18.2†

Source: Compiled and calculated from mortality data tapes for the years 1967 thru 1973 purchased from the National Center for Health Statistics of the Department of Health, Education, and Welfare, Public Health Service and from data in U.S. Bureau of the Census, U.S. Census of Population 1960: General Population Characteristics, Final Report PC (1) Minnesota, U.S. Census of Population 1970: General Population Characteristics, Final Report PC (1) Minnesota (Washington, D.C., U.S. Government Printing Office, 1962 and 1972) and U.S. Bureau of the Census, Current Population Reports, Series P-26 (Washington, D.C., U.S. Government Printing Office, 1973 and 1974).

\*Rates are per 100,000 population representing three year averages for the years specified and are age-adjusted to the total U.S. population for 1970.

<sup>1</sup>metropolitan counties include the central city counties of the four SMSAs in Minnesota

<sup>2</sup>small urban counties include the 19 counties in Minnesota which contain a city between 10,000 and 49,999 population

<sup>3</sup>rural counties include the 64 counties in Minnesota without a city of 10,000 or more population

†indicates a statistically significant difference at the 0.05 level. The test statistic used to compare the two proportions at two different points in time, under large sample approximation is the following:

$$z = \frac{\frac{n_1}{n_1 - n_2} - \frac{\lambda_1}{\lambda_1 - \lambda_2}}{\sqrt{\frac{(\lambda_1}{\lambda_1 + \lambda_2}) \left( \frac{\lambda_2}{\lambda_1 - \lambda_2} \right) / (n_1 - n_2)}}$$

where  $n_1$  is the number of suicides in 1967-1969, and  $n_2$  is the number of suicides in 1971-1973,  $\lambda_1$  and  $\lambda_2$  are the mean number of suicides at times 1967-69 and 1971-73 respectively. The  $\lambda$ 's are assumed to be the means of poison distributions.



Although it is not surprising to see significant increases in suicide rates for the younger females (0-44) because they are probably more greatly affected by new opportunities and the concomitant stresses, the reason for the large increase in suicide among rural women 45-64 is unclear. Perhaps rural women in this age group have unique problems associated with their geographic isolation and barriers to taking advantage of the publicized new opportunities.

The hypothesis that metropolitan women would experience the greatest increase in suicide was supported only for women 0-24. In the 25-44 age group, small urban women showed the greatest increase while for metropolitan women 45-64, suicide rates remained stable. When women in the two younger age groups are compared across areas, only the metropolitan women show a consistent trend of increase in suicide. Yet suicide rates for metropolitan (as well as small urban) males 0-44 also increased significantly. This over-all trend of increase among the younger age groups may be due to stresses growing out of the great social change of the 1960s that impacted most directly on the young.

Because by age group suicide rates for men are uniformly higher than for women, it is of great concern that several groups of males also experienced a substantial rise in suicide rates: There were significant increases in suicide rates for males age 0-24 in metropolitan, small urban, and rural areas; also for

males 25-44 in metropolitan and small urban areas; and for males 45-64 in small urban areas. Thus, one pattern emerging was the increase in suicide among small urban males 0-64 years of age. Perhaps this is related to rapid socioeconomic changes associated with the development of the small urban counties.

For males and females age 65 and over there were no significant suicide rate increases. This may be due to increasing economic stability growing out of expanded government programs to aid the elderly, such as medicare and social security. Nevertheless suicide rates for males 65 and over remain generally higher than for any other age-sex group.

### Conclusion

In the period 1967-1973, a time of great socioeconomic change, there were significant increases in suicide rates best seen by examining specific age-sex-area groups. If these trends continue, Minnesota's suicide rates may soon surpass the national average. Contrasting age groups reveals that generally the greatest increases in suicide occur among the young. In the 65 and over age groups there was either no increase or a significant decrease. Contrasting geographic areas reveals the greatest percentage of increases occur generally in non-rural areas with one major exception: rural females age 45-64 experience a large increase.

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# Tonsillectomy and Adenoidectomy Practice Patterns in Minnesota

## A Retrospective Multi-Hospital Audit

G. SCOTT GIEBINK, M.D.\*; TERRY E. THELL, R.R.A.† and Task Force on Tonsillectomy and Adenoidectomy Audit‡

The hospital records of 1,059 patients who had tonsillectomy, adenoidectomy, or adenotonsillectomy performed at 23 hospitals in Minnesota during a one-year period were audited to study medical and surgical practice patterns. Only 47% of records showed documentation of surgical justification describing the clinical history or failure of medical or surgical management of these operations. Anesthesia notes were incomplete in 64% of the records examined. Compliance with the individual operative management screening guidelines was greater than 90%. The overall complication rate for these procedures was 5.3%. The intra-operative hemorrhage complication rate was 3.4% while post-operative hemorrhage occurred in 1.6% of cases. Documentation of negative history of bleeding tendency, avoidance of aspirin-containing compounds before and after surgery and careful post-operative observations for bleeding might have reduced the hemorrhage complication rate.

ALTHOUGH LESS popular than it was earlier in this century, tonsillectomy and adenoidectomy is still one of the most frequently performed operations in the United States. It is estimated that 1 million tonsillectomies and adenoidectomies are performed in the United States each year, making the operation a \$375-500 million health industry.<sup>1</sup> While surgical justification of these procedures is controversial, potential risks of anesthesia and surgery, immunologic interference and possibly psychologic trauma have been identified. An ad hoc task force was convened by the Foundation for Health Care Evaluation to evaluate the medical and surgical practice patterns in Minnesota for these procedures. A key objective of this audit was to define the presently used norms for surgical justification and to determine the extent to which these norms varied among hospitals and physicians in Minnesota. In addition to addressing the surgical justification controversy, certain preoperative, operative and postoperative management criteria were selected to better understand practice patterns which might be associated with particular complications.

This study was supported by the Foundation for Health Care Evaluation, Minneapolis, Minnesota.

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## Material and Method

A task force consisting of a pediatrician, two otolaryngologists, a family practitioner and pediatric nurse developed the criteria and analyzed the results of this audit. A draft set of audit criteria was sent to all 36 hospitals in the Minneapolis-St. Paul metropolitan area and to 16 hospitals in northern Minnesota. Fifteen metropolitan and eight northern hospitals responded to the draft criteria with suggestions for modification and with agreement to participate in the audit.

Audit criteria were selected to permit evaluation of surgical justification norms: preoperative, operative and postoperative management; discharge status; length of stay; and complications. General guidelines used in developing these criteria came from the "Model Screening Criteria for Use by Professional Standards Review Organizations", proposed by the American Medical Association,<sup>2</sup> and from a multi-hospital audit of T & A performed in New Jersey.<sup>3</sup> The Minnesota audit included eight criteria or screening guidelines for tonsillectomy and six for adenoidectomy (Table 1).

Three additional surgical justification criteria were selected to detect patients where adenoidectomy or tonsillectomy would be indicated only in special circumstances. Nineteen preoperative, operative and postoperative management criteria were selected by the Task Force to represent appropriate management for patients undergoing these procedures. Eight



TABLE 1

Criteria Used in the Minnesota Multi-Hospital Audit of Patients Undergoing Tonsillectomy or Adenoidectomy	
	Compliance*
<b>Indications for Tonsillectomy</b>	
1. Any one of:	8%-100% (48%)
a. Suspected tonsillar tumor; or	
b. Peritonsillar abscess or documented history of peritonsillar abscess; or	
c. Diphtheria bacilli infected tonsil; or	
d. Tonsillar hypertrophy obstructing the airway causing: i) cor pulmonale; or ii) abnormality of breathing, swallowing or speech of at least three months duration; or iii) inadequate weight gain or weight loss due to dysphagia; or	
e. Four or more episodes of physician documented tonsillitis in preceding 12 months; or	
f. Chronic tonsillitis in persons 16 years of age and older with intermittent sore throat and persistent tonsillar exudate and tonsillar hypertrophy at least six months in duration.	
<b>Indications for Adenoidectomy</b>	
2. Any one of:	0-100% (60%)
a. Four or more episodes of acute otitis media in the preceding 12 months; or	
b. Four or more episodes of serous otitis media in the preceding 12 months; or	
c. Persistent serous, mucoid, secretory, or chronic otitis media in the preceding one month with failure of medical or surgical management; or	
d. Adenoid hypertrophy obstructing the airway causing: i) cor pulmonale; or ii) abnormalities of breathing, speech, swallowing, or dental occlusion; or	
e. Three or more episodes of documented adenoiditis or suspected Tornwaldts' cyst in the preceding 12 months in persons 18 years or older.	
<b>Indications for Adenotonsillectomy</b>	
3. Any one of:	0-100% (34%)
a. Documentation of at least one of the indications for tonsillectomy (a-f) plus at least one of the indications for adenoidectomy (a-e); or	
b. Documentation of 1.e) in patients less than 16 years of age.	
<b>Other Selection Criteria</b>	
4. No tonsillectomy in patients under three years of age.	87-100% 98%
5. No adenoidectomy in patients with velopharyngeal insufficiency.	100%
6. No tonsillectomy or adenoidectomy in patients with frank or submucous cleft palate.	100%
<b>Preoperative Management</b>	
7. Documentation of negative personal and family history of bleeding tendency or bleeding disorder, or documentation of a normal preoperative coagulation profile. (Coagulation profile = bleeding time; or prothrombin time and PTT and platelet count.)	0-100% (60%)
8. Nothing by mouth at least six hours prior to surgery.	8-100% (93%)
9. Penicillin or erythromycin pre and postop for all patients with: a) congenital heart disease; or b) history of acute rheumatic fever.	92-100% (99.9%)
10. Preop note by anesthesia.	8-100% (83%)
11. No T and/or A with low hemoglobin, high WBC or abnormal urinalysis. (Low hemoglobin = < 10, high WBC = > 15,000, abnormal UA = glucosuria, proteinuria, hematuria, or pyuria)	75-98% (92%)
12. Negative chest Xray within one week of surgery.	2-96% (73%)
<b>Operative Management</b>	
13. All T and/or A patients will have all of the following:	0-96% (56%)
a. Endotracheal intubation — unless local anesthesia	(99%)
b. Intraoperative IV fluids	(93%)
c. Minimal blood loss	(75%)
d. Microscopic pathology report on all patients 18 years of age or older	(91%)
e. Note describing absence of bleeding and general status at time of discharge from recovery room (Maximum blood loss in cc.s = body weight in pounds times 3)	(87%)
<b>Postoperative Management</b>	
14. No aspirin or aspirin-containing compounds during hospitalization.	47-100% (91%)
15. No blood or blood products (transfusions).	95-100%

\*Indicates range of compliance for all 23 hospitals in the study. Average of the compliance rates is shown in parentheses.



TABLE 1 (continued)

**Criteria Used in the Minnesota Multi-Hospital Audit of Patients Undergoing Tonsillectomy or Adenoidectomy**

	<b>Compliance*</b>
16. Documentation of observation postoperatively, at least every 8 hours for all of the following:	(99%) 0-100%
a. Bleeding status	(59%) (78%)
b. Airway status	(86%)
c. Ingestion of fluids	(88%)
d. Vital signs	(89%)
e. Voiding once in the postoperative period	(92%)
17. Post op note by anesthesia written within 24 hours of surgery but following discharge from recovery room.	8-100% (42%)
<b>Discharge Status</b>	
18. Patient afebrile or if febrile, plan for follow-up documented. (Afebrile = < 100° F oral or < 101° F rectal.)	72-100% (95%)
19. Absence of bleeding.	47-100% (83%)
20. Documentation that primary caretaker was instructed in all of the following:	0-82% (19%)
a. Not to administer aspirin-containing medications	(20%)
b. Diet restrictions	(67%)
c. Time and dose of pain medications	(69%)
d. Activity restrictions	(58%)
e. What to do if problems occur after discharge	(56%)
21. Patient given a clinic or office appointment to return within one month of discharge.	10-100% (81%)
22. No mortality.	100%
<b>Length of Stay</b>	
23. Preoperative ≤ 1 day.	98-100% (99.8%)
24. Postop stay ≤ 1 day for patients 16 years or younger, ≤ 3 days for patients 17 or older.	86-100% (97%)
<b>Complications</b>	
25. No hemorrhage. Hemorrhage = any patient readmitted or returned to operating room for control of bleeding or drop in hemoglobin of 2 gm. % from preop value.	88-100% (98%)
26. No vomiting or dehydration within seven days of discharge.	100%
27. No pneumonia or aspiration.	98-100% (99.9%)
28. No cardiac arrhythmia or arrest.	96-100% (99.8%)
29. No other complications.	(98%)

\*Indicates range of compliance for all 23 hospitals in the study. Average of the compliance rates is shown in parentheses.

discharge status elements were audited, as well as length of stay, complications and mortality.

A stratified, random method of patient selection was used to retrospectively audit records of patients who had tonsillectomy, adenoidectomy or adenotonsillectomy between August 1, 1976 and July 31, 1977. The audit sample of records from each hospital was based on the proportionate number of cases per physician in each of the three categories of surgery. Records were selected at random until the quota for each physician was met.

At each hospital, medical data analysts screened the medical records according to the modified criteria set developed by the task force. The data was collected and displayed for each hospital audit committee to review each variation and to determine if a deficiency in medical care existed. A narrative summary of each

case was also supplied to the task force, and variations were further reviewed by the task force.

### Results

The audit sample included 1,059 patients who had tonsillectomy, adenoidectomy or adenotonsillectomy performed during the one-year period. Tonsillectomy alone was performed on 326 patients, adenoidectomy on 170 patients and adenotonsillectomy on 563 patients. Eighty percent of patients were 16 years of age or younger, and 59% were between the ages of three and ten years. An equal number of males and females were selected. The 1,059 operations were performed by 218 physicians including 103 otolaryngologists, 95 family practitioners, 17 general surgeons and two pediatricians.

Evaluation of the justification for T and A surgery was hampered by lack of documentation of past



medical history in the hospital records. Fifty-three percent of all cases audited lacked documentation of the clinical history and failure of medical or surgical management necessitating surgical removal of tonsils or adenoids (Table 1). Of the documented cases, peritonsillar abscess, four or more episodes of tonsillitis, and chronic tonsillitis in persons 16 years of age and older accounted for the majority of justified tonsillectomy procedures (Table 2). Persistent otitis media failing medical or surgical management and adenoid hypertrophy causing an abnormality of breathing, speech, swallowing or dental occlusion were the most frequent justifications for adenoidectomy (Table 3). Only one-third of adenotonsillectomy procedures showed documentation of justification for surgery which met the screening guidelines (Table 4). Tonsillectomy was performed on 19 patients (1.7%) less than three years of age, and six of these children had medical record documentation of justification for surgery which met audit criteria. None of the patients audited had documentation of velopharyngeal insufficiency or cleft palate.

Forty percent of the patients had a T & A procedure without documentation of bleeding tendency or having had a normal coagulation profile (Table 1). Nine patients had documentation of a positive personal bleeding history but did not have documentation of a coagulation evaluation. Although only seven patients had documented or suspected congenital or rheumatic heart disease, five did not receive antimicrobial prophylaxis during T & A surgery. Thirty-one percent

of pediatric patients had a T & A procedure without documentation of a preoperative chest X-ray.

Ninety-four patients were given aspirin in the hospital following surgery, and the postoperative courses of three of these patients were complicated by hemorrhage (Table 1). Six patients, four adults and two children, received blood or blood products because of hemorrhage. Only 41% of hospital records documented compliance with all aspects of postoperative observation screened by these audit criteria. However, average compliance to the individual postoperative management elements exceeded 75% (Table 1). Twenty-one percent of records lacked documentation of observation for bleeding status, and 41% lacked documentation of observation of airway status postoperatively. Sixty-four percent of the hospital records lacked complete anesthesia notes. Preoperative anesthesia notes were missing from 5% of records, postoperative notes were missing from 46%,

TABLE 3

Surgical Justification — Adenoidectomy Procedure	
Justification Elements	Number (%) of cases
Four or more episodes of acute otitis media in the preceding 12 months	6 (4%)
Four or more episodes of serous otitis media in the preceding 12 months	8 (5%)
Persistent serous or mucoid or secretory or "glue" or chronic otitis media in the preceding one month with failure of medical or surgical management	30 (18%)
Adenoid hypertrophy obstructing the airway causing:	
i. Cor pulmonale	0
ii. Abnormalities of breathing, speech, swallowing, or dental occlusion	58 (34%)
Three or more episodes of documented adenoiditis or suspected Tornwaldt's cyst in the preceding 12 months in persons 18 years or older	0
No documentation of surgical justification	68 (39%)
Total	170 (100%)

TABLE 2

Surgical Justification — Tonsillectomy Procedures	
Justification Elements	Number (%) of Cases
Suspected tonsillar tumor	3 (1%)
Peritonsillar abscess or documented history of peritonsillar abscess	52 (16%)
Diphtheria bacilli infected tonsil	0
Tonsillar hypertrophy obstructing the airway causing:	
i. Cor pulmonale	1 (.3%)
ii. Abnormality of breathing, swallowing or speech of at least three months duration	6 (2%)
iii. Inadequate weight gain or weight loss due to dysphagia	0
Four or more episodes of physician-documented tonsillitis in preceding 12 months	63 (19%)
Chronic tonsillitis in persons 16 years of age and older with intermittent sore throat and persistent tonsillar exudate and tonsillar hypertrophy of at least six months duration	33 (10%)
No documentation of surgical justification	168 (52%)
Total	326 (100%)

TABLE 4

Surgical Justifications — Tonsillectomy with Adenoidectomy Procedure	
Justification Elements	Number (%) of Cases
Documentation of at least one of the indications for tonsillectomy plus at least one of the indications for adenoidectomy	96 (17%)
Documentation of four or more episodes of physician-documented tonsillitis in the preceding 12 months in patients less than 16 years of age	96 (17%)
No documentation of surgical justification	371 (66%)
Total	563 (100%)



and both pre and postoperative notes were absent in 13%. Seventeen hospitals showed variation rates to this criterion greater than 30%.

At the time of discharge, 61 patients (6%) were febrile and the charts of 183 patients (17%) showed no documentation of the absence of bleeding. Discharge instructions were incomplete or missing for 859 patients (81%), and 80% of records were incomplete because the admonition to avoid aspirin-containing compounds was not given to the patient or his caretaker.

All the hospitals audited found the pre- and postoperative length of stay guidelines sufficient. Only five cases varied from the one-day preoperative stay. Thirty of the 347 patients younger than 17 years, and two of the 212 patients 17 years and older had postoperative stays longer than the criterion.

The major complication disclosed in this audit was hemorrhage. Thirty-six patients (3.4%) had documented intra-operative hemorrhage with greater than a 10% loss of estimated blood volume, and 18 patients (1.7%) had postoperative hemorrhage. The hemorrhage complication rate was lower for adenoidectomy (2.9%) than for either tonsillectomy (4.3%) or adenotonsillectomy (5.9%). Of the 18 patients with postoperative hemorrhage, eight were returned to the operating room because of bleeding before discharge from the hospital, and nine were readmitted to the hospital because of bleeding following discharge. One patient had more than a 2 gm% fall on hemoglobin postoperatively but was not reoperated. Fifteen of these 18 patients also varied from one or more of the criteria that might have predicted postoperative hemorrhage. Six patients lacked documentation of a negative bleeding history or of a normal coagulation profile, two patients had no documentation of intra-operative blood loss, four lacked documentation of postoperative observation of bleeding status, one lacked documentation of absence of bleeding at discharge, three received aspirin postoperatively, and 13 patients or their caretakers were not instructed to avoid aspirin usage for one week after surgery.

Hemorrhage complication rates were calculated for physicians in the metropolitan area. Forty-two of 704 patients (6.0%) who had T &/or a surgery by 168 physicians had intra-operative or post-operative hemorrhage. The hemorrhage complication rate was highest for the group of 131 physicians performing fewer than six cases per year and was also high for the six physicians performing more than 20 cases per year (Table 5). There was no significant difference in the hemorrhage complication rates for otolaryngologists, general surgeons or family practitioners. Two patients had documented cardiac arrhythmia. One seven year old child had ventricular extra-systoles documented during surgery which responded to IV Lidocaine, and one five year old child had an electrocardiographic diagnosis of sinus tachycardia with a heart rate of 150/minute. A 23 year old patient who had a tonsillectomy performed for "tonsillar cellulitis" was readmitted four days postoperatively with pneumonia. There were no deaths. Thus, T & A surgery was complicated in 57 cases yielding an overall complication rate of 5.3%.

Minor differences in patient management were found on comparing the 15 metropolitan hospitals and eight northern hospitals. Eighty-six percent of metropolitan area patients had preoperative chest Xrays compared with 48% of the northern patients. The difference was due to fewer chest Xrays obtained on pediatric patients in the northern hospitals. In the northern hospitals, only 9% of patients were given discharge instructions which met all of the screening guidelines compared with 24% of metropolitan patients. Sixty-six percent of northern patients and 89% of metropolitan patients showed documentation that a follow-up office appointment was given. In all other respects, compliance rates to the screening guidelines were similar for northern and metropolitan hospitals.

### Discussion

The concept of multi-hospital area-wide medical record audit is a recently devised method for

**TABLE 5**  
**Hemorrhage Complication Rates by Number of Cases Per Physician\***

Number of Physicians	No. of Audited Cases per Physician	No. of Audited Patients	No. (%) of Patients with Intra-operative or Post-operative Hemorrhage
131	1-5	249	16 (6.4%)
19	6-10	139	7 (5.0%)
10	11-15	124	4 (3.2%)
2	16-20	37	2 (5.4%)
6	21-28	155	13 (8.4%)
168		704	42 (6.0%)



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identifying patterns of medical practice, comparing practice patterns among area hospitals and physicians, and providing a reasonable response to the public's call for health care accountability. This multi-hospital audit was initiated by the regional PSRO, the Foundation for Health Care Evaluation. Tonsillectomy and adenoidectomy was chosen for this audit because the Foundation believed that selection of patients for these procedures would reflect current medical practice patterns for two common pediatric illnesses, tonsillopharyngitis and otitis media, and preoperative, operative and postoperative management would reflect hospital and surgical practice patterns for commonly performed surgical procedures.

For most surgical procedures the pathologists' review of tissue specimens provides a measure of appropriateness of surgery. The tissue pathology report is not, however, particularly helpful in measuring appropriateness of T and A surgery in most cases. For these procedures, surgical justification has been based on documentation of frequency of tonsillopharyngitis and otitis media. As in previous audits of T and A<sup>3,4</sup> the Minnesota T & A audit was hampered by lack of documentation in the hospital records of surgical justification for tonsillectomy, adenoidectomy and adenotonsillectomy. Overall, 53% of cases did not have documentation of surgical justification detailing the clinical history or failure of medical or surgical management necessitating these operations. It is possible that the results of this audit would have been considerably different if documentation of previous physician observations had been recorded in the hospital record. Since this is a problem not unique to T & A, hospital medical record staff might discuss methods with their staff physicians for transferring pertinent outpatient data from physicians' offices to the hospital record.

It is not surprising that documentation of surgical justification was sparse since surgical indications for tonsillectomy and adenoidectomy consist largely of opinion with the exception of unusual cases of tonsillar tumor, diphtheria-infected tonsils, peritonsillar abscess, nasopharyngeal obstruction causing hypoxia or cor pulmonale, or when difficulty in swallowing interferes with nutritional status.

More fundamental is the lack of reliable data concerning efficacy of these surgical procedures when performed for recurring tonsillopharyngitis or otitis media. Only five prospective studies have been reported, and all were in agreement that tonsillectomy yielded some reduction in throat infections, but they disagreed as to whether adenoidectomy led to a

reduction in the frequency of otitis media.<sup>5-9</sup> All studies, however, suffered shortcomings in design or methods. A serious flaw was the exclusion of children most severely affected by tonsil or adenoid-related conditions.

In an effort to overcome the shortcomings of earlier studies, a study of T & A is currently in progress at the Children's Hospital of Pittsburgh.<sup>10</sup> Results indicate that undocumented histories of recurrent throat infection given by patients and parents do not validly predict the clinical features and patterns of frequency of throat infection during prospective observation.<sup>11</sup> Thus, physician documentation of tonsillopharyngitis seems particularly appropriate before subjecting children to tonsillectomy.

The Pittsburgh group has also reported preliminary results from a prospective randomized, controlled trial of adenoidectomy efficacy in recurrent otitis media. Study findings to date in 142 Children show similar frequencies of recurrent otitis and duration of middle ear effusion in the adenoidectomy and control groups.<sup>12</sup> The study is ongoing, and larger numbers of subjects and longer observation periods are required to determine with reasonable certainty whether adenoidectomy is efficacious. Two other recent reports, however, also showed no beneficial effect of adenoidectomy on reducing the frequency of otitis media with effusion when myringotomy alone was compared with myringotomy plus adenoidectomy.<sup>13,14</sup>

The audit also focused attention on the management of T & A patients reasoning that documentation of management would be confounded to a lesser degree by controversy than surgical justification. Compliance with the preoperative screening guidelines was greater than 85% for all criteria except evaluation of bleeding tendency, obtaining preoperative chest roentgenograms on children, and recording the preoperative anesthesia visit in the medical record. It seems particularly appropriate to record results of a normal coagulation profile or documentation of a negative personal and family history of bleeding tendency before performing surgery which has been associated with a hemorrhage complication rate of 3-7%.<sup>6-7</sup> A negative history for bleeding tendency is less expensive and more sensitive in detecting potential bleeding disorders than a coagulation profile. Patients with a positive history of bleeding tendency, and there were nine such cases in this audit, should have a coagulation evaluation performed before surgery. The failure to obtain preoperative pediatric chest roentgenograms may be justified since a negative pulmonary and



cardiovascular examination may be more predictive of anesthesia complications than the roentgenogram. It is of particular concern that five of seven patients with histories of congenital heart disease or rheumatic fever with heart disease did not receive antimicrobial prophylaxis during T &/or A surgery. It is known that surgery of the upper respiratory tract in patients with structural heart disease may be associated with transient bacteremia and endocarditis.<sup>15</sup> Antibiotic prophylaxis is indicated because it is not possible to predict which of these patients will develop this infection.

The Joint Commission on Accreditation of Hospitals requires both pre- and postoperative notes by anesthesia. The Accreditation Manual states that a post-anesthesia note made in the surgical suite or in the recovery room ordinarily does not constitute a post-anesthesia visit. However, the discharging physician can meet this requirement by writing an appropriate post-anesthesia note.

The overall documented complication rate for tonsillectomy and adenoidectomy in this audit was 5.3%. Thirty-six patients (3.4%) had documented intra-operative hemorrhage, and an additional 231 patients (22%) lacked documentation of operative blood loss. Eighteen patients (1.7%) had postoperative hemorrhage. The information collected suggests that hemorrhage might have been prevented by careful preoperative and postoperative management, that is, documentation of a negative history of bleeding

tendency, avoidance of aspirin before and after surgery, and careful postoperative observation of bleeding status. It is of particular concern that 94 patients received aspirin-containing compounds during their hospitalization. It is known that acetylsalicylic acid impairs platelet function, and that this effect is irreversible for that generation of platelets. Excessive bleeding due to platelet dysfunction caused by this drug may occur if an individual has an underlying hemostatic abnormality or has had recent surgery.<sup>16</sup> Other complications included two patients with cardiac arrhythmias and one child with postoperative pneumonia.

Only 26 physicians of the 168 audited in the metropolitan area had patients with hemorrhage complications. Hemorrhage occurred more frequently among patients who had surgery performed by physicians performing very few and for those performing a large number of T & A procedures. Hemorrhage occurred less often with adenoidectomy than with tonsillectomy or adenotonsillectomy.

Unfortunately, these results do not clarify the area-wide norms for appropriateness of T & A surgery due to lack of documentation of prior history in the hospital record. Significant variations were noted in the failure to obtain or document the history of a negative personal and family history of bleeding tendency or of performing coagulation profiles, and in the use of aspirin both pre- and postoperatively. Both of these variations were noted area-wide and may have contributed to cases of post-operative hemorrhage.

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# *from* *Division of Socio-Economic Affairs*

James H. Sova, Assistant Executive Vice President  
Lynn R. Gruber, Director, Department of Medical Services and Research  
George C. Lohmer, Jr., Director, Department of Health Planning  
Charles W. Wiger, Director, Department of Legislative Affairs

## **Legislative Affairs**

With the Legislature adjourned activity of the Department turns to agency implementation of newly passed laws. Preparation for the November elections and 1981 legislative session has begun.

The Department of Public Welfare held an initial information session May 13 to discuss rule-making to approve mental health centers and clinics for insurance reimbursement. Staff control and authorization of non-physician health personnel to provide reimbursable services for mental health centers and clinics are the major issues to be discussed over the next several months. MMA staff will participate in drafting the proposed rule to assure that patient privacy and quality care continue to be delivered through physician supervision.

During the next several months Legislative Affairs staff will meet with physicians in clinics and hospitals to discuss the 1980 session and emphasize the importance of political involvement and advance planning. From Ely to Luverne and Warren to Spring Grove the message "Join MINNPAC" is being spread. Work to draft legislation and prepare positions on issues will serve little purpose if friends of medicine are not elected to the 1981 Legislature.

## **Medical Services & Research**

### Health Data Collection Proposals

Due to the current interest in lowering health care costs, a number of organizations are interested in collecting health data from hospitals in an attempt to analyze the frequency of medical services rendered, cost of services, reason for service and other facts.

The Director of Medical Services & Research is monitoring a federally funded project residing with the Minnesota Hospital Association called the "Integrated Data Demonstration Project." This project would design, develop and implement an integrated data base including information from billings, related discharge abstracts and provider costs which could be accessible to multiple users. The ultimate



Lawrence M. Poston, M.D., Vice Speaker of MMA House of Delegates presenting testimony on the proposed new Veteran's Administration Health Center, to the Metropolitan Health Board.

Dr. Poston has recently been elected a Trustee from this District.



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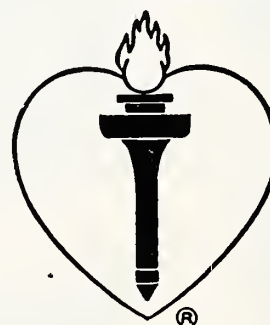
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goal of the project is to bring all Minnesota hospitals into the electronic data transmission system.

In recent months the Health Insurance Association of America (HIAA), representatives from local insurance companies, corporations, the Minnesota Department of Health, and representatives from the physician and hospital communities met to discuss the possibility of initiating a project whereby Twin City hospitals would agree to share health data abstract information among themselves for cost efficiency analysis and voluntary quality assurance patient review for patients not covered by federal health programs. In this project employers who provided their employees health insurance would be allowed to see the hospital abstracts to analyze the experience of health benefits utilized by their employees.

The HIAA project is only in the developmental stages. The grant held by the Minnesota Hospital Association, however, is approved and has two hospitals participating in the first year of the three year grant. The Minnesota Hospital Association has asked that the two groups work together in the gathering of health data.

Other developments in the area of health data include the recent creation by the Foundation for Health Care Evaluation of a Data Committee to deal with the future requests from the community for health data collected by hospitals. Donald C. Bell, M.D., MMA Trustee and Lynn R. Gruber, Director of Medical Services & Research, sit on this Committee.

### MMA Opposes Request for Waiver of HMO Requirements for Medicare Enrollees

SHARE, a St. Paul based HMO, has filed a request for waiver of HMO statutes and rules to allow Medicare recipients the use of SHARE as an alternative health care delivery mode. Waivers of required benefits are authorized for demonstration projects by Minn. Stat. 62D.30. George B. Martin, M.D., Chairman of the MMA Committee on Medical Service issued the Department of Health a response in which he objected to an HMO limiting significant health services to enrollees as potentially misleading. Granting of this request would initiate two levels of health services being offered under the roof of an institution which the public has heretofore understood to be a health maintenance organization, Dr. Martin stated. The general public's conception of an HMO is a health care delivery system offering full or comprehensive health care services. To permit an HMO to offer limited health benefits, may mislead potential enrollees into thinking that they will receive full or comprehensive health services.

## Health Planning

### MMA and Physicians' Metro Health Force Testify at Public Hearing on Veteran's Hospital Replacement

The Minnesota Medical Association, represented by Lawrence M. Poston, M.D., Vice-Speaker of the Minnesota Medical Association House of Delegates, and the Physicians' Metro Health Force, represented by A. Stuart Hanson, M.D., Chairperson of the Physicians' Metro Health Force Board presented testimony on April 30, 1980 to the Metropolitan Health Board on the proposed replacement of the Veteran's Administration Medical Center (VAMC) in Minneapolis.

The Minneapolis VAMC proposes to replace its facility by building a 845 bed hospital (of which 725 are hospital beds and 120 are nursing care beds) at a cost of \$221 million for facility construction, an estimated additional \$46 million for equipment, and \$5.5 million for a cyclotron.

The following points were made by both speakers: (1) Veterans should have the right to choose where they receive their care, (2) The PSRO program should be extended as a pilot study to the VAMC to ensure that all veterans receive quality care, (3) Recognition of the unique role of the VA in research, education, and patient care, (4) Support of a hospital of from 442 to 513 beds (exclusive of nursing care beds) at the Fort Snelling site, (5) Support for extensive sharing of specialized care resources between the VAMC and the University of Minnesota Hospital.

The Health Board's final recommendations were for a 609 bed hospital with a 40 bed nursing care unit, consolidation of the VAMC's radiation therapy and renal transplantation services with the University, increased participation of other hospitals in planning for activities such as open heart surgery and cardiac catheterization, and increased participation in PSRO activities. The Health Board's recommendations, as well as those of the MMA and PMHF, have been communicated to Congress which alone has the final decision-making authority. It is anticipated that Congress will make its decision on the initial planning appropriation by the end of May.



*Appropriateness Review Planning Regulations are Now Effective*

Add Appropriateness Review (AR) to your vocabulary. Appropriateness Review requires state and local planning agencies to pass judgment on the excess or shortage of existing institutional services. Most providers, of course, will be most concerned about decisions which state that a specific service is in excess of need.

There are no official enforcement powers related to HSA/SHPDA comments in the AR process. However, concerns have been raised about how these reviews will affect third party reimbursement, rate review decisions, CON/1122 decisions, hospital fund raising, and patient income. One interesting twist in the law may not allow any providers to vote on area-wide AR findings because of conflict of interest, but would allow them to vote on institutional-specific findings.

The first step in AR is the development of criteria to review specific services (e.g., Radiation Therapy), followed by an area-wide review of those services using the pre-determined criteria. If deficiencies are found, institution-specific findings and recommendations for corrective actions could be made.

As required by federal regulation, a plan for the assumption of responsibilities under AR was completed by the SHPDA and HSAs in April 1980. The services to be reviewed in the first of five cycles include: 1) End Stage Renal Disease, 2) Open Heart Surgery, 3) Cardiac Catheterization, and 4) Megavoltage Radiation Therapy.

*Significant HSA and Emergency Medical Services Program Funding Cuts Predicted*

The Office of Management and Budget, in its revised federal budget for fiscal 1981, proposes a 30 percent cut in grants to Health Systems Agencies (HSAs). This is a reduction from \$124.7 million to \$86.7 million. State agencies would face a budgeted decrease from \$35 million to \$32.5 million, a decrease of 7.1 percent. The magnitude of these cuts could force some HSAs to close, while others would concentrate only on their regulatory functions, such as Certificate of Need and Appropriateness Review (see accompanying article).

The Emergency Medical Services Program is also slated for significant cuts. Revised fiscal 1981 figures slated reduction in funding from \$36 million to \$24 million. To accomplish this, there are indications that all grants which focus primarily on improvements to the Advanced Life Support Systems (called 1204 grants), would not be funded. In Minnesota, this would mean the Metro EMS Program could be terminated as early as July 1, 1980, while the Northeast Minnesota EMS Program could be terminated July 1, 1981. There is some discussion that the Metro EMS Program could receive limited funding directly from the Metropolitan Council or other private sources.

*Physician Representation on the Statewide Health Coordinating Council*

Each year the terms of one-third of the members of the Statewide Health Coordinating Council (SHCC) expire. The terms of two physician members expired in January (Leslie A. Syverson, M.D., who was appointed to the SHCC as a representative from the Min-Dak Health Service Area, and Vernon L. Sommerdorf, M.D., St. Paul, who served as the Chairperson of the SHCC). Under the leadership of Dr. Sommerdorf, the SHCC grappled with substantive issues and developed the first State Health Plan.

The MMA Board of Trustees nominated Drs. Vernon L. Sommerdorf, St. Paul, and Richard J. Frey, Minneapolis, for the single at-large provider position vacancy. Governor Quie selected Dr. Frey from the numerous provider nominees to serve in this position. Governor Quie also appointed George R. Pettersen, M.D., Commissioner of Health, as the new Chairperson of the Statewide Health Coordinating Council. James H. Kelly, M.D., St. Cloud, is continuing his term as a SHCC member nominated as a representative of the Central Minnesota Health Service Area.



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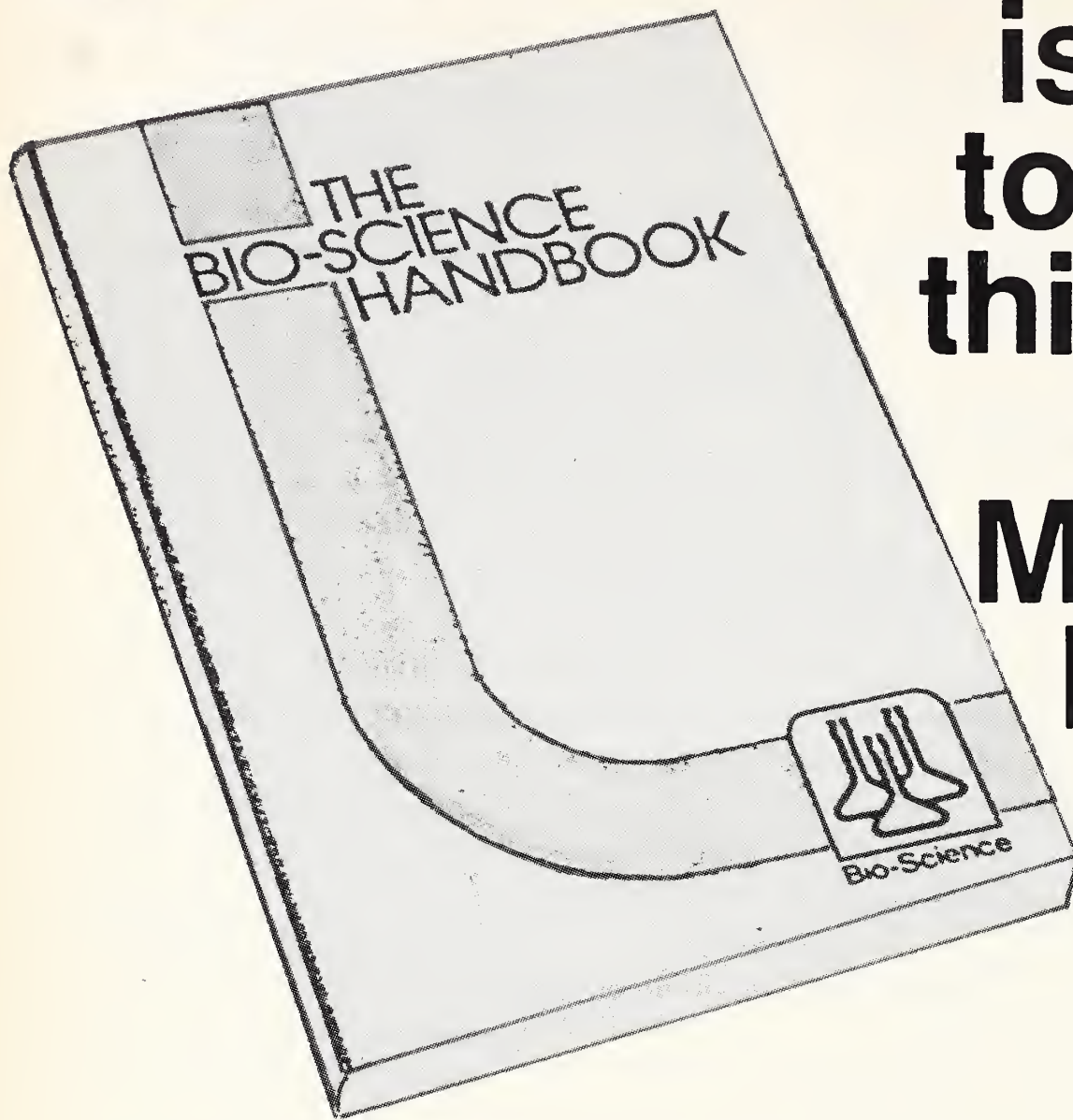
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# President's Letter



## Minnesota Medical Insurance Exchange

The word is "go." At its closing session on May 22, 1980, the House of Delegates of the Minnesota Medical Association authorized the formation of a physician-owned liability company to be known as Minnesota Medical Insurance Exchange.

The target date for activation of the Company is October 1, 1980. Prior to that time, a legally required surplus of \$1,500,000.00 must be obtained from physicians who will be purchasing insurance from the company. An individual physician's contribution will be proportional to his/her premium. This contribution will range from \$905.00 for a Class I physician to \$6,025.00 for a Class VII physician. The surplus amount will be reduced 10% for those physicians who contribute prior to September 1, 1980, in order to encourage early commitment. After this initial surplus contribution physicians will have no further financial obligation to the Company other than payment of premiums.

Our company's premiums are anticipated to be significantly lower than premiums currently in effect. Combining both the initial surplus contribution and first year premium, total costs to an individual physician will be competitive with premium rates currently in effect.

Further, one of the major advantages of a physician-owned company is its ability to effect underwriting and risk management procedures which should lead to further economies.

With your support the Minnesota Medical Association has spent a great deal of time and effort in the development of this new insurance program. Specific information concerning the program, its coverage, and its costs will soon be made available to you. Let me urge all of you to keep abreast of the development of your company over the next few, most critical months.

A handwritten signature in cursive script that reads "John K. Meinert M.D.".

**John K. Meinert, M.D.**  
President  
Minnesota Medical Association



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Anusol-HC Cream is also indicated for pruritus ani.

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**Warnings:** The safe use of topical steroids during pregnancy has not been fully established. Therefore, during pregnancy, they should not be used unnecessarily on extensive areas, in large amounts or for prolonged periods of time.

**Precautions:** Symptomatic relief should not delay definitive diagnoses or treatment.

If irritation develops, Anusol-HC Suppositories and Anusol-HC Cream should be discontinued and appropriate therapy instituted.

In the presence of an infection the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Care should be taken when using the corticosteroid hydrocortisone acetate in children and infants.

Anusol-HC is not for ophthalmic use.

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bedtime for 3 to 6 days or until inflammation subsides. Then maintain patient comfort with regular Anusol Suppositories.

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# Candidacy



Robert T. Kelly, M.D.

Dr. Robert T. Kelly, after a long career in medical affairs in the Range County Medical Society, the Minnesota Medical Association, and the AMA, is a candidate for the Board of Trustees of AMA.

Bob has served as an AMA Alternate Delegate and Delegate for twelve years in the House and chaired the MMA delegation. He was elected to the Council on Medical Service in 1974 and was recognized there for his leadership by being elected successively Vice-Chairman and Chairman of that Council. He headed an ad hoc committee on PSRO of the Council. He is a member of the National PSRO Advisory Council; served on the AMA Speaker's Bureau; and chaired the Ad Hoc Committee on Practice Evaluation.

He is former President of the North Central Medical Conference.



# Editorial

## Messages, Modifiers and Marshall McLuhan

Regulation of metabolic processes is a complex phenomenon occurring at multiple levels in biological systems and involving innumerable intermediaries. The endocrine hormones play a critical role in these biochemical regulatory functions. Classical paradigms have focused on the hormone itself as the key effector in the interaction with target structures. More recent models have emphasized the concept of the hormone receptor as the critical element in the transmission of this chemical information. The scheme of the release of a specific hormone into the circulation and its transport, on specific carrier molecules, to a distant target site, where it interacts with intracellular or cell surface receptors to result in specific effects, is most familiar. Endocrine information is perceived as being encoded within with the subtle and discrete molecular structure of the hormone. This structural specificity allows the endocrine substance to conform with the correspondingly specific receptor configuration and resulting from this interaction is a sequence of events which transfers information into the biologic expression identified as the hormone's effect.

Interposed between hormone and effect is a transducer sequence of prodigious design. Hormone receptors are metabolically active and dynamic systems which can influence their own production, confirmation, specificity and affinity. The degree and duration for which a hormone may be present and influence a receptor site is itself under variable control. Factors at a distance from the hormone-receptor complex can influence these processes as well as the local interactions of divalent and hydrogen ions. Previously dormant enzymatic systems, with their own complex systems of regulation are activated and may result in conformational changes in the receptor or the production of secondary messenger substances which further transport the information of the endocrine signal to other levels of regulation.

These secondary effectors interact with intracellular protein kinase systems mediating conversion of inert precursors into active products. Others will enter the cell nucleus and interact at multiple levels with the genetic material and its modulating nucleoproteins. Molecular transformations within the genome mediate transcriptional and translational events which further modify and amplify the endocrine information to more

specific expression.

The manifestation of clinical endocrine disorders is consequently not represented simply by the degree of activity of the particular gland or the measurable level of a given hormone in the circulation. The response of the biologic system is the result of the endocrine message it receives and its ability to process the information encoded within the signal. A multiplicity of modifiers play an intervening role influencing ultimate hormonal expression.

The clinician must be concerned with disorders in which normal or elevated levels of hormone may be present, but the patient manifests signs of endocrine deficiency. Such conditions of end organ insensitivity are related to the absence or modification of receptors so the endocrine signal is stopped before complete transmission. Disruption of the endocrine signal can occur anywhere along the sequence of hormone action. Specific clinical entities have already been described for many peptide and steroid hormones (i.e. nephrogenic diabetes insipidus, pseudohypoparathyroidism, male pseudohermaphroditism, insulin resistant diabetes mellitus, vitamin D insensitivity and Laron Dwarfism with insensitivity to growth hormone) and a large number are yet to be described with regard to the thyroid hormones, gonadotrophins, adrenal corticoids and ACTH.

Many conditions have already been identified as sub-types related to events which are prereceptor or postreceptor. Defects may occur as the result of absent protein kinases, absent genetic information for the hormone-receptor complex to interact with, inability to generate a secondary messenger or an abnormal ionic milieu within the cell depriving essential cofactors such as calcium or magnesium from facilitating critical chemical steps.

The hormone itself may be released from the endocrine gland in an abnormal structural state. Many peptides are secreted as larger prohormones which require cleavage of inert fragments in order to be biologically active and bind to their receptor. Failure of this process or even earlier events in biosynthesis, may release larger pre-prohormone secretory products and produce clinical endocrine deficiency states. Such entities have already been described for ACTH, parathyroid hormone and insulin and probably exist for



## EDITORIALS

growth hormone as well. Abnormal structural sequencing of peptide hormones may also occur, resulting in biologically inactive molecules. In steroidogenesis, important enzymes essential for modifying specific molecular positions may be absent or of decreased activity and produce steroid molecules with diminished biological activity.

Lastly transport of hormones from their sites of secretion to their sites of action requires binding substances in the circulation. Structural modification

or quantitative changes in the levels of available transport carrier molecules can produce a variety of endocrine abnormalities.

In contemporary clinical endocrinology, the medium is the message. The expression of the endocrine information transcends the hormone itself and is the consequence of a multiplicity of biological circumstances.

David Raoul Brown, M.D.  
Symposium Editor

### Reference

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### Acknowledgment

The editors wish to acknowledge the invitation of the following authors to be included in this symposium but due to prior commitments they were unable to participate.

Robert A. Ulstrom, M.D. Department of Pediatrics, University of Minnesota, Minneapolis.

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Alvin Hayles, M.D. Sections of Pediatrics and Internal Medicine, Mayo Clinic, Rochester.

Lawrence Riggs, M.D. Section of Clinical Endocrinology, Department of Medicine, Mayo Clinic, Rochester.

Richard Doe, M.D. Department of Internal Medicine, Veteran's Administration Hospital, Minneapolis.

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### Cover Drawing "The Endocrine Cell"

Jennifer Raskob is a medical illustrator recently graduated from The College of St. Catherine's. She has created a visual fantasy of the endocrine cell as the ultimate unit of hormone synthesis and mechanism of endocrine hormone action.

Peptide hormones are seen binding to their specific cell surface receptors. Adenylate cyclase enzymes present within the cell membrane convert ATP to the secondary messenger cyclic AMP. This in turn binds to the receptor component of inactive protein kinase enzymes within the cytosol. A free catalytic component is then released as an active protein Kinase which initiates the enzymatic conversion of substrate precursors to a final product. This is the basic model for the mechanism of action of peptide hormones and catecholamines.

Steroid hormones are present within the cytosol of their target tissues where specific receptors for these substances are also present. Specific binding of the steroid results in conformational changes in the resulting complex and its transport to the nucleus of the target cell. The association of the steroid-receptor unit with the nucleoprotein of the genetic material, results in activation of the DNA leading to the transcription of the genetic information as a specific messenger RNA. This m-RNA passes out of the nucleus to the microsomal portion of the cytosol where the information is further translated by the ribosomes into a specific polypeptide sequence of amino acids. This resulting protein is a product of the steroid cell inaction which mediates the hormone's ultimate effect.

The thyroid hormones produce their effects by similar interactions after binding with specific nuclear receptor sites.



# The Endocrine Laboratory and Its Role In the Practice of Clinical Endocrinology

MICHAEL W. STEFFES, M.D., Ph.D.\*

The clinical endocrine laboratory makes a substantial contribution to the diagnosis and management of patients with endocrine diseases. In its optimal application this involvement rests upon a sound technical capability and an active communication between the personnel in the laboratory and the clinical endocrinologists who use the facility.

THE PRACTICE OF modern clinical endocrinology demands the availability of a wide variety of laboratory procedures (Tables 1 and 2). In understanding the pathophysiology of endocrine disease, the hormone(s) from the diseased gland or the controlling gland must be measured. It may also be important to measure the biologic activity or efficacy of the hormone(s) — i.e. the urinary excretion of cyclic-adenosine monophosphate (cAMP) in hyperparathyroidism (Table 2). The appropriate selection of endocrine tests can mean an

effective diagnostic procedure for the patient with a conscientious effort to control costs. Active cooperation between the health-care personnel dealing directly with the patient and those working in the laboratory provides the medium through which both technical and clinical exigencies can be weighed.

## Methods Employed in the Clinical Endocrine Laboratory

The competitive protein binding assay — most often the radioimmunoassay (RIA) — provides the methodology to measure hormones in serum or urine. The pervasive use of immunoassay techniques in

\*Director, Clinical Chemistry and Endocrine Laboratories, Department of Laboratory Medicine and Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

TABLE 1

Hormones In Plasma Measured By Immunoassay (Primary Radioimmunoassay) and the Problems to Which Measurement of the Hormones May be Applied

<u>Hormone</u>	<u>Problem(s) in Which the Hormone Most Often is Measured</u>
<u>Thyroid Gland</u>	
Total Tetraiodothyronine (T <sub>4</sub> )	Hypothyroidism and Hyperthyroidism
Total Triiodothyronine (T <sub>3</sub> )	Hyperthyroidism only
Thyrotropin of Thyroid Stimulating Hormone (TSH) T <sub>3</sub> -Uptake	Hypothyroidism only An indirect indicator of thyroid binding proteins — useful in interpreting T <sub>4</sub> and T <sub>3</sub> levels (see reference 5)
<u>Adrenal Gland</u>	
Cortisol	Excessive production of cortisol (Cushing's syndrome) and deficient production of cortisol (Addison's disease)
<u>Gonadal Function</u>	
Lutropin or Luteinizing Hormone (LH)	
Follitropin or Follicle Stimulating Hormone (FSH)	Gonadal failure
Testosterone	Virilization in women
<u>Pituitary Gland</u>	
Somatotropin or Growth Hormone	Somatotropin deficiency in children; Somatotropin-secreting adenoma in adults
Prolactin	Prolactin-secreting adenoma
Corticotropin or Adrenal Cortical Stimulating Hormone (ACTH)	ACTH-secreting adenoma
<u>Parathyroid Gland</u>	
Parathormone (PTH)	Hyperparathyroidism
<u>Islets of Langerhans</u>	
Insulin	Hypoglycemia caused by excessive production of insulin



endocrinology stems from the availability of an "antibody" (really a family of immunoglobulin molecules) raised in an animal. The technology used to immunize animals often successfully provides an antibody with extraordinarily high levels of both sensitivity and specificity frequently associated with a high titer (or the presence of a large number of immunoglobulin molecules). Successful harvest of a good antibody may yield a volume of reagent to last the average laboratory several decades.

Hormones circulate in plasma at very low concentrations, in solution with many constituents present in significantly greater amounts. In assaying either polypeptide or steroid hormones, careful consideration must be given to the possible interference from non-hormonal species with similar structures. These technical difficulties and the need to accomplish many measurements within a short time obviate the utilization of many standard techniques to measure protein and steroid hormones. Thus, for many hormones the antibody and a radiolabeled form of the hormone with a high specific activity may be combined in a RIA as the *only* procedure capable of measuring the hormone. The theory and practical rationale applied to competitive protein binding assays have been extensively reviewed.<sup>1-3</sup> Since the RIA maintains a dominant role in the measurement of hormones, this discussion centers upon the technical exigencies and vicissitudes of the RIA.

The two most important reagents in any RIA are the antibody (raised in an animal as described above) and a radiolabeled form of the hormone. Several techniques covalently bind (sometimes in substitution) a radioactive isotope (usually <sup>125</sup>I, and for some steroid assays <sup>3</sup>H) to a very pure form of the hormone. The labeled hormone (H\*) may then be utilized as a sensitive indicator of the amount of unlabeled hormone (H) present in the specimen (Figure ). Routinely H and H\* compete for binding sites on the antibody, the level or

hormone in the sample (H) inversely affecting the amount of H\* bound. As H increases, the binding of H\* to the antibody decreases. Once the reaction in Figure has reached completion, the antibody bound H\* and/or the free H\* must be separated and counted in a scintillation counter (a gamma scintillation counter containing a NaI crystal for <sup>125</sup>I and a liquid scintillation counter for <sup>3</sup>H). Each instrument converts the radioactive emission (γ-ray for <sup>125</sup>I and β-particle for <sup>3</sup>H) to a photon of light which registers an electronic impulse in a photomultiplier tube. Many different techniques can physically separate (usually by precipitation) the bound and unbound H\* prior to counting. Convenience, efficiency and cost determine which procedure is selected. The relationship between the amount of bound-H\* and the level of H in the standards eludes precise mathematical description, but

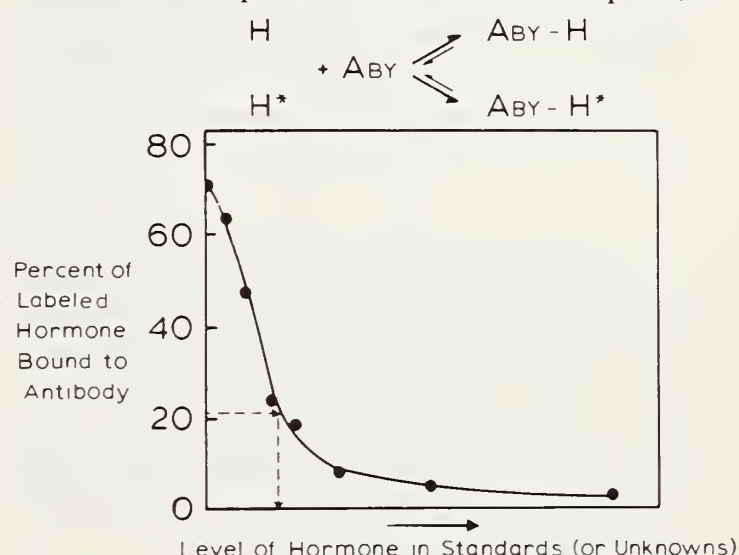


Figure — Schematic presentation of a radioimmunoassay (RIA). To a serum (or urine) sample containing an unknown amount of the hormone (H) to be measured, antibody (ABY) to the hormone and labeled hormone (H\*) are added. When incubated, H and H\* will compete for binding sites on the ABY. Following the incubation of the components, the bound and unbound portions of H\* may be determined (using a variety of techniques). Several different expressions (in this case percent H\* bound) may be calculated and plotted versus the level of H in the standards to yield a standard curve. The percent bound in an unknown may then be utilized to estimate the concentration of H in that sample (dotted line).

**TABLE 2**  
Substances (Primarily Hormones) In Urine and the  
Endocrine Problems to Which Their Measurement May be Applied

<b>Steroids</b>	
Cortisol and its Metabolites	Cushing's disease or Addison's disease
17 Ketosteroids	
17-Hydroxyprogesterone and its Metabolites	Congenital Adrenal Hyperplasia
Estriol	Maintenance of the fetus and the placenta
<b>Polypeptides</b>	
Chorionic Gonadotropin	Confirmation of pregnancy
<b>Others</b>	
Catecholamine Metabolites	Catecholamine-secreting tumors
Cyclic-Adenosine Monophosphate (cAMP)	Hyperparathyroidism



very good computational approximations programmed into a desktop computer efficiently reduce and convert the raw data from the counters to levels of hormone in the samples.

The proceeding commentary applies broadly to all radioimmunoassays whether they measure proteins, steroids or other molecules. With certain substances (notably the steroid hormones) preliminary purification procedures are necessary to remove constituents present in the samples at sufficient concentration to cross-react in the RIA. Thus if not eliminated, constituents cross-reacting in the RIA will spuriously *elevate* the measured level of the hormone.

Although the RIA with radiolabeled reagents has continued to be the primary procedure in the clinical endocrine laboratory, other labels (enzymes are a promising class) may permit more flexibility in performing hormonal measurements and the facility of having a longer-lived and safer non-radioactive labeled hormone. The primary application of enzyme-labeled immunoassays has been in the monitoring and measurement of drugs in serum and urine.<sup>4</sup> The molar concentrations of drugs necessary to provide therapeutic efficacy often greatly exceed the levels of hormones normally found in serum. Hormones present in relatively high molar concentrations (i.e., total thyroxine and total triiodothyronine in serum) may be measured with enzyme-labeled immunoassays. However, hormones present in much lower concentrations remain detectable only with RIAs.

Technologies other than immunoassays show promise to supplant RIAs in the measurement of some hormones. Chromatographic methods combined with physical-chemical detectors (i.e., high performance liquid chromatography and gas-liquid chromatography) may effectively measure steroids and catecholamines. However, the sensitivity of most currently available detectors limits the application of these techniques.

### Quality Control — within and outside the Laboratory

Most RIAs utilized in the measurement of hormones

\*This kind of problem concerning measurement of hormones most often involves steroid assays in which substances with structures very similar to the measured constituent may be present in very high levels. As an example, prednisone — or even more significantly, prednisolone — will be measured in the cortisol RIA causing inappropriately high values. Problems in cross-reactivity may also arise in the RIAs of polypeptide hormones. Chorionic gonadotropin may be inappropriately measured in the RIA for luteinizing hormone. In fact an "unmeasurably" high luteinizing hormone value may often signify pregnancy. In our laboratory this recently happened with a sample from a woman who was being evaluated for "long-standing infertility". An initially negative response came from the resident on the station concerning the question of a possible pregnancy in the woman. With confirmation of her new clinical status there was obviously no need to continue her infertility workup.

have relatively high coefficients of variation (CV — calculated as the standard deviation of multiple determinations of a single, uniform specimen divided by the mean of the determinations, usually expressed as percent). CVs may be calculated as intra-assay (several values from one assay) or inter-assay (many levels over an extended period of time). The inter-assay CV extended over many months provides an index of assay reproducibility most closely applicable to the practice of clinical medicine, wherein the same hormone may be measured repeatedly at several-month intervals in the patient. Estimated over intervals approaching or exceeding one year, CVs in most RIAs will range from under 10 to 20%. This variation within the assay reflects slightly different assay conditions over the extended period of time. Most likely the largest effect on a RIA stems from variability in lots of labeled hormone. With RIAs for steroid hormones, the pre-RIA separation procedures add to the variability of the assay. Thus of the hormonal assay, the steroid RIAs evince the greatest CVs. With the potentially large CV inherent in most RIAs, a laboratory must perform its assays under consistent conditions (i.e., with non-labeled materials unchanged even as to lot numbers of antibodies) for periods of months and hopefully years.<sup>5</sup>

In practice the clinical endocrine laboratory should proceed to check the quality of its results by including quality control samples with each assay and establishing mean and standard deviation for each lot of control serum. When measured levels of the hormone in the control samples fall outside the mean  $\pm$  2 standard deviations, strong consideration should be given to repeating the assay.

### Clinical Relevance of Reported Results

The clinician — by appreciating the limitations of the laboratory and knowing how the laboratory performs its procedures — becomes an important resource (and partner) in the optimal provision of laboratory results to the patient. By being aware of results apparently outside his or her routinely experienced norms, the clinician may alert the laboratory to problems that may *not* be recognizable through its usual quality control procedures. For example, an assay may consistently and accurately measure a hormone in quality control samples. Yet the presence of interfering drugs or other hormones in patient samples may significantly alter the levels measured and potentially reported *and* remain undetected by usual quality control procedures.\* Most often the



appropriate development of an assay accounts for potential circumstances causing significant interference; however, in any good laboratory an alert staff working with perspicacious users of the laboratory should *expect* to find problems arising that were not initially expected. The difficulties grow when a problem is *not* recognized.

Active consultation between physicians on the stations and their counterparts in the laboratory permits a careful and efficient selection of laboratory tests in the evaluation of endocrine disease. Carefully considered application may optimize the utilization of tests on an outpatient basis, limiting inpatient testing to problems that can only be addressed by a professional staff in the hospital (e.g., the administration of drugs and collection of specimens during a prolonged evaluation of adrenal function). A high level of cooperation among physicians whose responsibilities spanned the ward and the clinical laboratory spurred

the development of a rapid RIA for 17-hydroxyprogesterone, permitting laboratory confirmation of a presumptive clinical diagnosis within 24 hours of receipt of a serum or urine specimen.<sup>6</sup> With other problems in the <sup>131</sup>I treatment of metastatic thyroid carcinoma (optimized by monitoring TSH levels), with the complicated evaluation of adrenal function, and during the administration of pergonal contraceptive therapy (ideally monitored with estradiol measurements) — the appraisal of the need for rapidly reported results allows coordination among the personnel on the station and in the laboratory. With this communication a normal pattern of work may be maintained in both areas while selectively delivering some results in the most efficient manner. Without such interaction excellent clinical management and laboratory testing may still occur, but the outcome for the patient may not be quite as good as it would with the cooperation.

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### MINNPAC Shifts into High Gear for Fall Elections

The Interspecialty Council working with the MINNPAC Board launched a major membership effort for MINNPAC in June. Members of each specialty society were contacted by a colleague already belonging to MINNPAC, with the message — JOIN UP. With MINNPAC membership well below 20%, the highest priority has been given to increasing membership.

It is being stressed that each dollar contributed to MINNPAC returns many more dollars in benefit to medicine's image. It allows MINNPAC to support candidates in those districts in the state which do not have physicians. Therefore, it is necessary to participate organizationally even if you already support a local candidate of your choice. By allowing MMA staff to attend candidate and party fundraisers, the MINNPAC dollar ties in the political contribution arm with the policy arm of medicine.

According to L. Ashley Whitesell, M.D., MINNPAC Chairman, the most important task takes place after the filings close on July 17 when a determination is made which candidates to support. While early signals are available from many districts, the close of filing is the true indicator of who is vying for which seat. Active membership involvement in providing information about candidates is greatly appreciated, added Whitesell. Nothing is more valuable in assisting MINNPAC on candidate selection than to have direct input from the candidate's home newspaper or physician.



# Mechanisms of Thyroid Hormone Action

CARY N. MARIASH, M.D.\* and JACK H. OPPENHEIMER, M.D.\*

Thyroid hormone action is initiated when triiodothyronine ( $T_3$ ) binds to its specific protein receptor in the cell nucleus. The  $T_3$ -nuclear receptor complex then generates a signal which increases messenger RNA's coding for specific proteins known to be induced by thyroid hormones. Both the  $T_3$ -nuclear receptor as well as the signal generated by the  $T_3$ -nuclear receptor complex are modulated by hormones and other factors in producing the ultimate tissue response to thyroid hormone.

**T**HE NEED FOR thyroid hormone for proper growth, development, and maintenance of body functions has been recognized for nearly a century. However, an understanding of the mechanism by which thyroid hormones act has eluded thyroidologists until recently. The difficulty in understanding thyroid hormone action arose in part from the multitude of biochemical processes stimulated by thyroxine without an apparent unifying concept. Nevertheless, two recent developments have led to major advancements in our understanding of thyroid hormone action: (1) the development of radio-immunoassay techniques allowing easy measurement of the more metabolically active hormone, triiodothyronine ( $T_3$ ) and, (2) a recognition of the  $T_3$ -nuclear receptor as the cellular site of initiation of thyroid hormone action.

With the ability to measure  $T_3$ , it has now been shown that plasma  $T_3$  is primarily derived from the conversion of thyroxine ( $T_4$ ) in peripheral tissues such as the liver and kidney. The thyroid hormones are transported in the plasma by several binding proteins. These proteins, however, have no major significance in the action of thyroid hormones. For example, during pregnancy there is a marked increase in the plasma thyroxine binding globulin with a consequent increase in the total  $T_4$  concentration; however, the concentration of free  $T_4$  in pregnancy remains unchanged and the patient remains euthyroid. There are also binding proteins in the cell cytoplasm which, like the plasma binding proteins, are relatively unimportant in thyroid hormone action. For further discussion of thyroid hormone production and metabolism in health and disease, refer to several recent reviews.<sup>1,2</sup>

We should like to review the evidence which implicates a  $T_3$  binding protein in the nucleus of the cell as the site of initiation of thyroid hormone action.

\*Division of Endocrinology and Metabolism, Department of Medicine, University of Minnesota, Minneapolis, Minnesota.

This work has been supported in part by NIH Grant AM 19812-03. CNM is a recipient of NIH Research Fellowship 1-F32-AM05880-01.

In addition, we shall discuss some of the factors which appear to modulate the signal produced by the  $T_3$ -nuclear receptor complex. Finally, we shall briefly discuss several clinical implications of the modulation of the  $T_3$ -nuclear receptor and its signal.

## Establishment of Nuclear Receptors for $T_3$

In order for a binding protein to be considered a specific receptor for a hormone, it must exhibit several properties. Three of these properties are: (1) a limited capacity and high affinity for the hormone, (2) a high correlation between the affinity of the receptor for hormone analogs and the biologic activity of these analogs, and (3) the presence of these receptors in tissues which are hormone responsive. However, demonstration of these properties, though highly suggestive, does not prove conclusively that the binding protein is a true receptor. Such proof would entail the demonstration that purified receptor initiates hormonal action in an *in vitro* reconstituted cell free system. This clearly has not been accomplished with the  $T_3$ -nuclear receptor.

The presence of limited capacity binding sites for  $T_3$  in the nucleus of liver and kidney was first described in 1972.<sup>3</sup> Subsequently, similar limited capacity binding sites were found in all thyroid responsive tissues in the rat;<sup>4</sup> in rat pituitary tumor cells;<sup>5</sup> human tumor cells;<sup>6</sup> and normal human liver, kidney and white cells.<sup>7,8</sup> These binding sites are located in the cell nucleus and consist of nonhistone protein bound to chromatin. The protein has a molecular weight of approximately 50,000 daltons and displays similar physico-chemical properties in both man and rat.<sup>7,9,10</sup>

The physiologic relevance of these binding sites was confirmed by studies correlating the relative binding affinity of thyroid analogs with the thyromimetic activity of these analogs. For example, reverse  $T_3$ , moniodotyrosine, and diiodotyrosine have very little affinity for this binding protein and they have virtually



no thyromimetic activity. This relationship holds true for virtually all other analogs which have been tested. Two exceptions are triiodothyroacetic acid (triac) and  $T_4$ . Triac binds as tightly to the nuclear receptor as  $T_3$ , but has less biologic potency than  $T_3$ . This discrepancy is explained by the more rapid metabolism of triac *in vivo*. Since triac is metabolized more rapidly than  $T_3$ , the residence time of triac on the nucleus will be less than that of  $T_3$  after equal doses are injected.

As opposed to triac, which binds to the receptor as tightly as  $T_3$  but has less biologic activity,  $T_4$  has more biologic activity than expected based on its relative affinity for the receptor. That is,  $T_4$  has only 1/10 the binding affinity for the nuclear receptor relative to  $T_3$ , but is approximately 1/3 as potent as  $T_3$ . The explanation for this difference is the fact that  $T_4$  is converted to  $T_3$ . Thus the two exceptions, triac and  $T_4$ , when analyzed in terms of their metabolic fate, actually help to prove the rule that analog binding affinity correlates with biologic potency.

Further evidence indicating the nuclear binding sites are specific receptors for  $T_3$  derives from receptor occupancy-response relationships. Two  $T_3$  responsive hepatic enzymes,  $\alpha$ -glycerophosphate dehydrogenase and malic enzyme, are synthesized maximally only during the period after  $T_3$  administration when the receptor sites are fully occupied. With progressive metabolism of  $T_3$  the receptor sites are depleted of  $T_3$  and the rate of synthesis of new enzyme decreases.<sup>11</sup>

Finally, as mentioned previously, these binding sites have been demonstrated to be present in those tissues which are known to be thyroid responsive, such as the liver, kidney and pituitary. On the other hand, tissues which do not appear to be responsive to thyroid hormone, such as the spleen and testes, have very few specific binding sites per cell. An interesting exception is the brain. This tissue appears to have a large number of  $T_3$ -nuclear receptors, and yet is not thyroid responsive in the adult. Perhaps the nuclear receptors are needed only during early life when thyroid hormone is needed for proper development and maturation of the brain. Another and perhaps more likely possibility is that a thyroid hormone response is present but has not yet been identified.

The large body of evidence presented which identified the  $T_3$ -nuclear receptor as the site of initiation of thyroid hormone action does not exclude the possibility that there are extra-nuclear sites of thyroid hormone action. Nevertheless, reports which have proposed mitochondrial<sup>12</sup> sites have not been confirmed.<sup>13</sup> Membrane effects of  $T_3$ <sup>14-16</sup> have required large nonphysiologic concentrations of  $T_3$ .

### Modulation of the $T_3$ -Nuclear Signal

Since the establishment of the  $T_3$ -nuclear receptor as the site of initiation of thyroid hormone, there have been many reports demonstrating changes in nuclear receptor numbers under differing pathophysiological conditions. For example, administration of pharmacologic doses of glucagon, starvation, and partial hepatectomy all decrease the number of hepatic  $T_3$ -nuclear receptors per cell.<sup>17-20</sup> Furthermore, the hepatic malic enzyme response to  $T_3$  is partially inhibited under these conditions. In addition to modulation of the number of hepatic  $T_3$ -nuclear receptors as noted above, Samuels has shown that  $T_3$  itself can cause a depletion of its nuclear receptor in a rat pituitary tissue culture line, GH1 cells.<sup>21</sup> This, however, has not been demonstrated in tissues of the intact animal.

Even more intriguing than modulation of the number of receptors is the modulation of the signal produced by the  $T_3$ -nuclear receptor complex. There are three specific mRNAs that have been identified as products of the  $T_3$ -nuclear complex signal; growth hormone mRNA from GH1 cells,<sup>22,23</sup>  $\alpha$ <sub>2</sub>U-globulin mRNA from the liver of male rats,<sup>24,25</sup> and rat hepatic malic enzyme mRNA.<sup>26</sup> Interestingly, thyroid hormone is not the only factor involved in the stimulation of these mRNAs. In tissue culture, glucocorticoids can enhance 2-5 fold GH mRNA induction by thyroid hormone. Likewise,  $\alpha$ <sub>2</sub>U-globulin mRNA induction by thyroid hormone is modulated by both glucocorticoids and androgens. These steroids must be present in order that thyroid hormone can induce  $\alpha$ <sub>2</sub>U-globulin mRNA. Unfortunately, the physiologic role of  $\alpha$ <sub>2</sub>U-globulin is unknown.

We have recently shown an interaction between carbohydrate feeding and thyroid hormone administration on malic enzyme induction and its specific mRNA.<sup>26,27</sup> This is a physiologically relevant system inasmuch as malic enzyme is important for hepatic lipogenesis. Lipogenesis is stimulated during periods of carbohydrate excess for energy storage, and thus it is not surprising that malic enzyme is stimulated by a high carbohydrate diet. However, the hypothyroid state inhibits the ability of the high carbohydrate diet to induce malic enzyme. On the other hand, the  $T_3$  induction of malic enzyme in hypothyroid animals is enhanced approximately five-fold by the administration of a high carbohydrate diet. Thus,  $T_3$  induction of malic enzyme requires a carbohydrate factor, and carbohydrate induction of malic enzyme requires  $T_3$ . This interaction of carbohydrates with  $T_3$  is not due to a carbohydrate-induced alteration in  $T_3$  metabolism or in



T<sub>3</sub>-nuclear receptor affinity. Furthermore, the T<sub>3</sub>-induction of malic enzyme is not due exclusively to a T<sub>3</sub> mediated alteration in carbohydrate metabolism but appears to be a direct effect of the hormone itself.

The site of interaction between the carbohydrate signal and the T<sub>3</sub> signal has been identified from measurements of malic enzyme mRNA. A high degree of correlation has been found between the level of malic enzyme, the rate of synthesis of malic enzyme, and the steady state level of malic enzyme mRNA. Therefore, carbohydrate feeding must interact with the T<sub>3</sub>-nuclear receptor signal at a postreceptor site to stimulate the formation of malic enzyme mRNA.

### Clinical Implications of the T<sub>3</sub>-Nuclear Receptor

The concept of the T<sub>3</sub>-nuclear receptor as the site of initiation of thyroid hormone action has several important clinical implications. Recently, Bantle et al. have shown that heart rate, Achilles tendon relaxation time, and serum cholesterol are linearly correlated with T<sub>3</sub>-nuclear occupancy.<sup>28</sup> That is, the overall thyroidal status of a patient is directly related to the nuclear-T<sub>3</sub> concentration which can be calculated from the plasma T<sub>3</sub> level. The linear correlation between nuclear-T<sub>3</sub> occupancy and several diverse response characteristics helps to establish the heretofore elusive unifying concept of thyroid hormone action.

A discrepancy in two situations where the free T<sub>3</sub> concentration does not predict the clinical status of the

patient can be better understood by examining the nuclear T<sub>3</sub> signal. The first anomaly is the Refetoff syndrome.<sup>29</sup> These patients are euthyroid, and yet they have very high free T<sub>3</sub> concentrations. Recently, Bernal et al. have shown that the thyroid hormone resistance exhibited by these patients is due to a decrease in the strength of T<sub>3</sub>-nuclear binding.<sup>30</sup> With less specific nuclear binding, higher free hormone concentrations are needed to normalize the concentrations of occupied T<sub>3</sub>-nuclear receptors.

The other clinical situation in which there is a difference between T<sub>3</sub> concentrations and the predicted thyroidal status is the euthyroid sick patient.<sup>31</sup> These patients have low T<sub>3</sub> concentrations but appear to be clinically euthyroid based on parameters such as TSH level, heart rate, skin texture, and deep tendon reflexes. Postreceptor factors such as those demonstrated for malic enzyme, 2U-globulin, and growth hormone, may also serve to modulate these thyroid hormone-responsive parameters. Thus it appears possible that the signal from a diminished T<sub>3</sub>-nuclear concentration is appropriately amplified by postreceptor factors to produce clinical euthyroidism.

Further research is needed to identify the precise nature of the post-receptor modifying factors as well as the mechanism by which the T<sub>3</sub>-nuclear receptor initiates mRNA synthesis. These studies should then allow us to more fully understand the pathophysiologic abnormalities associated with the hyperthyroid and hypothyroid states in man.

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# Clinical Disorders of Pituitary and Thyroid Hyperfunction

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Acromegaly, hyperprolactinemic amenorrhea/galactorrhea, and pituitary-dependent Cushing's syndrome are caused by pathological hyperfunction of the pituitary gland with resultant excessive production of, respectively, growth hormone, prolactin, and adrenocorticotropin. In many cases the etiology will be a small, functioning pituitary adenoma and the treatment of choice transsphenoidal, microsurgical, selective pituitary adenectomy. More radical pituitary surgery, radiation therapy, or bromocriptine therapy may be advisable in certain cases.

Grave's disease and toxic nodular goiter are the most frequent causes of pathological thyroid hyperfunction. Thyrotoxicosis may also occur, transiently, in subacute, silent, or Hashimoto's thyroiditis. Where indicated, confirmation of the significance of elevated levels of total and free (directly or indirectly measured) thyroxine can be obtained by measuring the serum triiodothyronine and by performing a thyrotropin releasing hormone (TRH) test. Preferred methods of treatment for sustained hyperthyroidism continue to be blocking drugs and radioactive iodine.

**R**ECENT ADVANCES in basic and clinical science have significantly improved our ability to diagnose and treat hyperfunctional disorders of the pituitary and the thyroid glands.

## Pituitary Disease: Hyperfunction

The clinical disorders of pituitary function to be considered here include acromegaly<sup>1</sup>, amenorrhea-galactorrhea<sup>2</sup>, and Cushing's syndrome<sup>3</sup>. The underlying etiology of these disorders remains to be elucidated. Present evidence indicates that at the time of clinical presentation, the excessive production of growth hormone (GH) in acromegaly, of prolactin (PRL) in cases of markedly hyperprolactinemic amenorrhea/galactorrhea, and of adrenocorticotropin (ACTH) in pituitary-dependent Cushing's syndrome originates from functional and generally solitary adenomas or microadenomas of the pituitary gland.

### Acromegaly

In acromegaly<sup>1</sup> the initial diagnostic step remains a careful clinical evaluation for: (1) signs and symptoms

of GH excess, (2) possible general pituitary insufficiency, and (3) pituitary-tumor mass-effect. Clinical findings are listed in Table 1. Of particular importance is the soft tissue growth resulting in excessive fleshiness and 'puffiness' of the hands, especially in the thenar areas. The failure of the serum GH level to decline to less than 5 ng/ml<sup>1</sup>, and generally to less than 2-3 ng/ml<sup>4</sup>, during a standard three hour glucose tolerance test remains the principle biochemical finding required for the diagnosis of active acromegaly. This may be supplemented by an abnormal rise in serum GH following intravenous thyrotropin releasing-hormone (TRH) administration<sup>5</sup> and elevated basal levels of serum Somatomedin-C<sup>6</sup>, pro-

**TABLE 1**  
**Selected Signs and Symptoms in Acromegaly**

#### Symptoms:

1. increased glove, ring, shoe, or hat size
2. tingling of fingers (carpal tunnel syndrome)
3. excessive malodorous sweating
4. headache
5. arthritis and arthralgias

#### Signs:

1. fleshiness of the hands and feet
2. typical acromegalic facies (coarse features, thick lips, large nose, frontal bossing)
3. large tongue
4. prognatism with overbite of lower incisors and separation of teeth

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duced by the liver under the influence of GH and responsible for many of the clinical findings of acromegaly.

#### *Hyperprolactinemic Amenorrhea/Galactorrhea*

Suppression and stimulation tests are of limited value because the response of the serum PRL level to stimulation, by TRH, or to suppression, by L-DOPA, is often qualitatively similar in both pituitary tumor and non-pituitary tumor patients. This is unfortunate since hyperprolactinemia can result from a number of non-neoplastic causes. Quantitatively, the percent change from baseline is frequently less in patients harboring a prolactin secreting pituitary tumor. Of more practical importance is that the likelihood of a pituitary tumor increases with the magnitude of the elevation of the basal serum prolactin level. Recent studies<sup>2</sup> suggest that the majority of patients with serum prolactin levels greater than 100 ng/ml will have pituitary tumors<sup>2</sup> and probably all patients with basal serum PRL levels greater than 300 ng/ml will have pituitary tumors<sup>2</sup>. Patients with serum prolactin levels significantly less than 100 ng/ml, however, may still harbor pituitary microadenomas.

#### *Cushing's Disease*

When Cushing's syndrome<sup>3</sup> is pituitary-dependent, it is referred to as "Cushing's disease". The underlying pathology in nearly all cases of "Cushing's disease" at the time of clinical presentation appears to be pituitary neoplasia and not primary hypothalamic dysfunction. The diagnosis of Cushing's syndrome will generally be made by history, physical examination, measurement of the 24 hour urinary free cortisol and the performance of the overnight dexamethasone suppression test. Once Cushing's syndrome has been diagnosed, the presence of a pituitary tumor rather than an adrenal tumor or ectopic ACTH production from a nonpituitary tumor is suggested by the maintenance of a significant degree of suppressibility of cortisol production by high doses of exogenously administered dexamethasone. It is also suggested by the ability of metyrapone, a blocker of the 11-hydroxylation step in cortisol synthesis, to stimulate net total adrenal-steroid production. In the normal individual (Figure 1), metyrapone administration causes the serum cortisol to fall, thus diminishing the usual glucocorticoid-produced negative feedback on the ACTH-secreting pituitary cells. This results in a rise in serum ACTH and a resultant increase in the serum level of the metabolite proximal to the 11-hydroxylation block, 11-desoxycortisol or "Compound S". The metabolites of Compound S (CPDS), like those of cortisol, are

measured in the 17OH corticosteroids (17OHCS) of the urine. Thus, following metyrapone administration, serum Compound S and the 24 hour urinary 17OHCS rise in the normal individual. The rise is accentuated in pituitary-dependent Cushing's syndrome. Since most adrenal tumors and nonpituitary tumors producing ectopic ACTH function autonomously and have already suppressed the normal pituitary's ability to produce ACTH, there is no net rise in the urinary 17OHCS following metyrapone. In Cushing's disease, bilateral adrenal hyperplasia results from a greater than normal but still submaximal stimulation of the adrenal cortices by endogenous ACTH. This is demonstrated by the marked increase in the total adrenal steroid production produced by either exogenous ACTH or the further elevation of endogenous ACTH following metyrapone. While the basal 8 AM serum ACTH is usually suppressed in Cushing's syndrome due to an adrenal tumor or markedly elevated in ectopic ACTH syndrome, in Cushing's disease it may be only moderately elevated or within normal limits<sup>7,8</sup>. The 24 hour integrated value should be greater than normal. The absolute or percentage rise in serum ACTH following metyrapone administration, in some patients with Cushing's disease, may actually be less than the rise seen in normal individuals<sup>9</sup>. This may reflect the ability of a small elevation in serum ACTH in patients with already hyperplastic adrenal glands to bring about the same effects as larger amounts of ACTH in patients with normal sized adrenal glands. The stimulatory effects of the ACTH rise will usually not completely overcome the 11-hydroxylation block. It is therefore reasonable to conclude that in pituitary-dependent Cushing's syndrome, the quantitatively "modest"

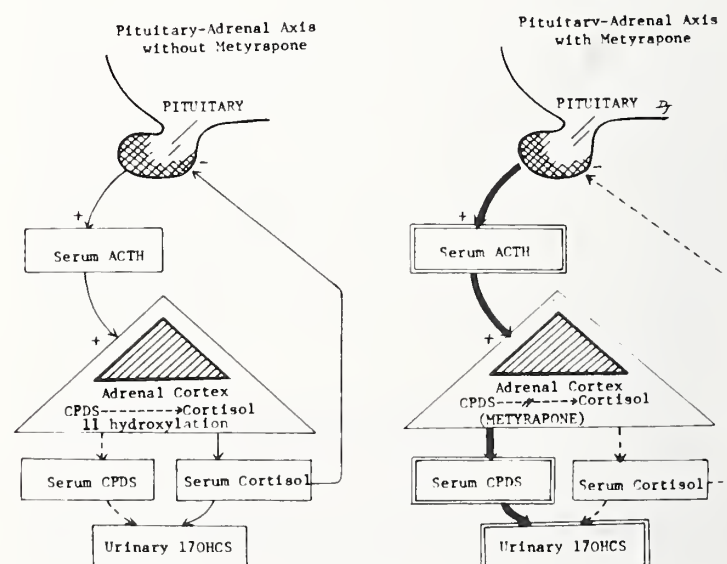


Fig. 1 — Metyrapone Test in the Normal Individual.



response of ACTH to Metyrapone suggests the underlying pathophysiology of clinical Cushing's disease is not the resetting or cybernetic readjustment of a finely tuned, structurally intact, hypothalamic-pituitary-adrenal axis. It is, instead, the neoplastic transformation of pituitary cells with subsequent diminution and sluggishness of cellular response to both the repressive effects of glucocorticoid excess and the stimulatory effects of glucocorticoid lack.

Analogous to the case of the acromegalic, where a rise in growth hormone follows injection of TRH<sup>5,10</sup>, the patient with Cushing's disease may show a rise in serum ACTH following TRH administration.<sup>11</sup>

**TABLE 2**  
**Causes of Hyperprolactinemia**

- I. **Physiological**
  1. Breast stimulation
  2. Postpartum
- II. **Pathological**
  1. Hypothalamic disorders or surgery
  2. Pituitary tumors or surgery
  3. Primary hypothyroidism
  4. Chronic renal failure
  5. Ectopic production by non-pituitary tumors
  6. Thoracic wall stimulation
- III. **Pharmacological**
  1. Psychotropic drugs (phenothiazines and tricyclic antidepressants)
  2. Oral contraceptives
  3. Antihypertensive drugs (reserpine and Methyldopa)
  4. Cimetidine

#### *General Evaluation of Pituitary Functional Reserve*

Once pituitary hyperfunction resulting in acromegaly, amenorrhea-galactorrhea, or Cushing's disease is diagnosed, investigations will be required to evaluate general pituitary function. The choice and interpretation of the tests to be performed must be done with caution. For example, apart from any deficiencies of pituitary hormones resulting from pituitary-tumor mass-effect, levels of serum prolactin in hyperprolactinemic amenorrhea-galactorrhea will interfere with normal hypothalamic-pituitary-gonadal function. Similarly, elevated levels of serum cortisol in Cushing's disease may interfere with a variety of tests, including those for evaluation of growth hormone reserve and of hypothalamic-pituitary-gonadal and hypothalamic-pituitary-thyroidal function.

The necessity for thorough pituitary testing in patients with these disorders is, in part, related to what will frequently be the treatment of choice: transnasal, transsphenoidal, microsurgical, selective pituitary adenectomy.<sup>12</sup> This involves utilization of an

operating microscope by an experienced neurosurgeon for the purpose of selectively removing a small pituitary tumor without destruction of adjacent, normal, pituitary tissue. Under these circumstances it will usually be advisable to assess general anterior pituitary function both before and after pituitary surgery.

Endocrine tests that have been found useful in assessing anterior pituitary functional reserve are listed in Table 3.

**TABLE 3**  
**General Evaluation for Anterior-Pituitary Functional Reserve**

I. <u>Growth Hormone (GH):</u>	1. Basal and post L-DOPA stimulated serum GH 2. Basal serum Somatomedin-C
II. <u>Prolactin (PRL):</u>	Basal and post TRH stimulated serum PRL
III. <u>Gonadotrophins (LH and FSH):</u>	1. Basal LH, FSH, estradiol (female) and testosterone (male) 2. Supplementary: basal and post clomiphene citrate stimulated LH, FSH, estradiol (female) and testosterone (male) 3. Supplementary: basal and post LRH stimulated LH and FSH
IV. <u>Thyrotropin (TSH):</u>	1. Basal serum thyroxine and T <sub>3</sub> resin uptake 2. Basal and post TRH stimulated serum TSH
V. <u>Adrenocorticotropin (ACTH):</u>	Basal and post Metyrapone stimulated serum ACTH, 11-desoxycortisol, serum cortisol, and 24 hour urine collection for 17-hydroxycorticosteroids.

#### *Radiology in Pituitary Disease*

Recent radiological advances have facilitated the evaluation of pituitary disease and its target-organ effects: polytomography of the sella turcica<sup>13</sup> may reveal changes suggesting the presence of a microadenoma; computerized tomography (CT) may show suprasellar extension of a pituitary tumor and, in some cases even an intrasellar mass<sup>12,14</sup>; and computerized tomography of the adrenal glands,<sup>15</sup> possibly supplemented by NP-59 radioactive adrenal scanning<sup>16,17</sup>, may facilitate adrenal tumor localization and the differentiation between an adrenal tumor and pituitary-tumor-produced bilateral adrenal hyperplasia in a patient presenting with Cushing's



syndrome. When large tumors that impinge upon the optic chiasm are present, visual field determination may also reveal abnormalities.

#### *Transsphenoidal Pituitary Surgery*

Almost all cases of clinical acromegaly and pituitary-dependent Cushing's syndrome, and the majority of cases of markedly hyperprolactinemic amenorrhea/galactorrhea, result from hormone production by adenomas or microadenomas (less than 10 mm in diameter) of the pituitary gland. Thus, transsphenoidal selective removal of the pituitary tumor, with preservation of normal pituitary tissue, has increasingly become the predominant treatment for these disorders<sup>12</sup>. This is true even when the presumed microadenoma is not seen during preoperative radiological evaluation. It is essential that the endocrine work-up be thorough and the diagnosis correct. Large pituitary tumors, with marked suprasellar extension, may require transfrontal surgery. Also, some tumors treated transsphenoidally are too large or too invasive to allow "selective" removal with preservation of normal pituitary tissue.

The success rates in Cushing's disease are excellent.<sup>9,18,19,20</sup> This is true also in hyperprolactinemia when the tumor is small and the serum prolactin elevation relatively modest.<sup>20,21,22,23</sup> The achievement of a true "cure" (the abolition of GH response to TRH and the normalization of basal and glucose-suppressed growth hormone levels)<sup>20,24,25</sup> in acromegaly would appear to be somewhat more difficult.<sup>4</sup> Furthermore, the recurrence rate may be higher. Thus, some patients may require more than one transsphenoidal sellar exploration. (Therefore, in selected cases, it may even be advisable to proceed directly to total sellar "clean-out" and supplemental radiation therapy in view of the long-term ill effects on the musculoskeletal and cardiovascular systems and life expectancy in this disease.) Long term recurrence rates following selective pituitary microadenectomy remain to be established.

Figure 2 illustrates two patients recently evaluated pre and postoperatively by the author. In each case transsphenoidal selective pituitary microadenectomy resulted in complete clinical and biochemical cure of Cushing's disease and complete preservation of normal pituitary function. Biochemical data is presented elsewhere.<sup>9</sup> Preoperative polytomography and CT scans with the recently available, advanced CT scanner (General Electric 8800) were read as "normal" in both cases.

#### *Radiation and Drug Therapy in Pituitary Disease*

Radiation therapy continues to play a role in some

pituitary tumor cases, but it is usually secondary to surgery. In hyperprolactinemic amenorrhea-galactorrhea where a pituitary tumor is not thought to be present or where it is present but definitive neurosurgical therapy is not desired, bromocriptine,<sup>29,30</sup> a dopaminergic agonist, may be used. This drug will generally lower the serum prolactin, often to normal levels, in both pituitary tumor and nonpituitary tumor patients. There are reports that it may decrease tumor size. Bromocriptine has also been used in acromegaly. Medical treatment for Cushing's disease (metyrapone, aminoglutethimide, opDDD, and/or cyproheptadine) has limited long-term utility, numerous disadvantages, and is generally not advised. A finite course of medical therapy in acromegaly, hyperprolactinemic amenorrhea-galactorrhea, or Cushing's disease rarely, if ever, results in a permanent cure.

#### **Thyroid Disease: Hyperfunction**

Recent advances have improved our ability to diagnose and treat hyperfunctional disorders of the thyroid gland. Elements of the patient's history and physical examination will generally have suggested the presence of thyrotoxicosis. Confirmation requires appropriate biochemical testing. The initial laboratory test ordered is the serum thyroxine, which will usually be elevated. Since it is the free rather than the bound thyroxine which is "active", the amount of thyroxine binding globulin present must also be considered. Thus, a T<sub>3</sub> resin uptake test is also obtained: an increased uptake of exogenous I<sup>125</sup> — labeled T<sub>3</sub> by the added resin suggests a decrease in free TBG binding sites and thus an increase in free as well as total thyroxine. Correction of the total T<sub>4</sub> by the T<sub>3</sub> resin uptake results in the "thyroxine index".<sup>31</sup> A true measurement of the free thyroxine can also be obtained.

#### *Triiodothyronine (T<sub>3</sub>) in Thyrotoxicosis*

Where further confirmation of thyrotoxicosis is required, the level of endogenous serum T<sub>3</sub> should also be determined. Although the thyroid secretes T<sub>3</sub> directly, the majority of T<sub>3</sub> results from the peripheral conversion of T<sub>4</sub>. In fact, T<sub>4</sub> functions largely as a "prohormone" for T<sub>3</sub> since T<sub>3</sub> is considerably more potent than T<sub>4</sub> and accounts for most of the thyroid hormone activity. It is T<sub>3</sub> which primarily binds to the intranuclear thyroid hormone receptor. T<sub>3</sub> nuclear receptors have recently been identified in two major thyroid-hormone target organs in man,<sup>32</sup> the liver and the kidney. In almost all cases of thyrotoxicosis, there will be an elevation of T<sub>3</sub>, or at least the level of





Pre-op



Post-up

14-year-old boy with Cushing's disease secondary to an ACTH-secreting pituitary microadenoma, treated by transsphenoidal pituitary surgery. (By permission).



Pre-op



Post-op

36-year-old woman with Cushing's disease secondary to an ACTH-secreting pituitary microadenoma, treated by transsphenoidal pituitary surgery. (By permission).

Fig. 2 — Response to transsphenoidal selective pituitary microadenomectomy in Cushing's disease.



presumed free  $T_3$  where corrections for binding are made by simultaneous consideration of the  $T_3$  resin uptake value. In most cases of hyperthyroidism, there will be an increase in the  $T_3$  to  $T_4$  ratio. This is particularly accentuated in  $T_3$  toxicosis, where the patient is thyrotoxic secondary to excess  $T_3$  production while the total  $T_4$  is still within normal limits.

#### TRH Test in Endogenous Hyperthyroidism

In some patients with mild thyrotoxicosis,  $T_4$  RIA,  $T_3$  resin uptake,  $T_4$  index or free  $T_4$ , and  $T_3$  RIA determination will show only borderline abnormalities. Occasionally, a patient with a goiter will have laboratory tests suggesting increased thyroid function but will have only equivocal symptoms or physical findings of thyrotoxicosis. In both of these cases further laboratory confirmation of the presence of thyrotoxicosis is indicated. Although it is reasonable to assume that the serum TSH would be suppressed in thyrotoxicosis, most clinical laboratories do not have assays sensitive enough to differentiate between a normal and a suppressed basal serum TSH. Under these circumstances the test of choice is the TRH stimulation test:<sup>33</sup> a baseline serum TSH is obtained and 500 mcg of TRH are injected intravenously; 30 minutes later a second serum TSH is drawn. In patients with even mild thyrotoxicosis, the persistently elevated levels of endogenous thyroid hormone will be suppressing TSH output by the pituitary. Exogenously administered TRH will not overcome this suppression and the serum TSH will not rise significantly following TRH injection. An absent TSH response to TRH will thus confirm the presence of functionally significant hyperthyroidism when baseline thyroid hormone levels are only borderline or when there is an apparent disparity between these laboratory values and the clinical presentation. The TRH test in thyrotoxicosis is illustrated in Figure 3.

#### TRH Test in Iatrogenic Thyroid Suppression

It should parenthetically be noted that the TRH test may also be useful when it is desirable to document iatrogenic complete suppression of the pituitary-thyroidal axis in the treatment of thyroid cancer<sup>34</sup> and in some cases of goiter suppression. In differentiated thyroid cancer (papillary or follicular histology) near total thyroidectomy is usually performed. Once the patient's serum TSH has risen to beyond the normal range and is thus capable of inducing maximal uptake of exogenously administered  $I^{131}$  by any metastases present, a total body  $I^{131}$  scan is obtained. Additional  $I^{131}$  is then administered to ablate any remaining normal or abnormal thyroid tissue and any thyroid

cancer metastases.<sup>35,36</sup> The patient is then placed on a suppressive dose of synthetic thyroxine, a rule-of-thumb being 1 mcg of thyroxine per pound of body weight for "replacement"<sup>34</sup> and an additional 25-50 mcg of thyroxine to insure "suppression". Since approximately 80% of circulating  $T_3$  is derived from peripheral conversion of  $T_4$  in the normal individual and since the half life of  $T_4$  is one week while that of  $T_3$  is one day, the administration of pure synthetic thyroxine rather than thyroid extract, a synthetic combination of  $T_4$  and  $T_3$ , or  $T_3$  alone is considered preferable both in treating hypothyroidism and in suppressing the pituitary-thyroidal axis. Four to six weeks following the beginning of suppressive therapy, serum  $T_4$ ,  $T_3$  resin uptake, and  $T_3$  are determined. If the patient has no findings of thyrotoxicosis on this dosage and the levels of  $T_4$  and  $T_3$  are at the upper end of the normal range or minimally elevated, a TRH test is performed. If there is no significant rise in TSH, then the pituitary-thyroidal axis is suppressed and the patient is continued on this dose of Synthroid until six weeks before the next  $I^{131}$  total body scan, when the patient is switched to shorter acting triiodothyronine ( $T_3$ ), which is discontinued four weeks later, two

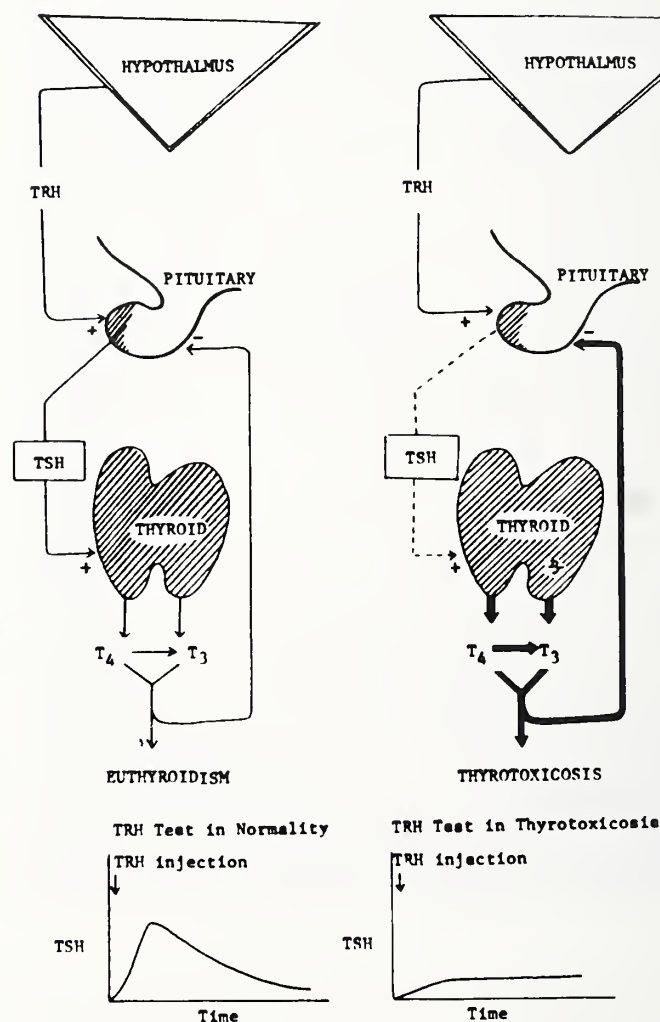


Fig. 3 — TRH Test in Thyrotoxicosis.



weeks before the scan is performed.

### *Differential Diagnosis and Mechanisms in Thyrotoxicosis*

In general the thyroid scan (technetium or  $^{123}\text{I}$ iodine) or 24 hour radioactive iodine uptake is of limited utility in the diagnosis of hyperthyroidism. However, a single "hot" nodule or multiple "hot" nodules in a thyrotoxic patient will indicate that the cause of thyrotoxicosis is, respectively, either an autonomously hyperfunctioning nodule or multiple autonomous hyperfunctioning nodules rather than Grave's disease. In Grave's disease<sup>37</sup> the goiter is diffuse and results from stimulation of the thyroid gland by thyroid stimulating immunoglobulins (TSI), substances which have been measured quantitatively by several research laboratories and whose levels correlate with the degree of activity of the disease process.<sup>37</sup> The TSI molecules combine with the TSH membrane receptors in the thyroid gland and result in cellular stimulation with resultant goiter formation and thyroid hormone production. Grave's disease is thus an autoimmune phenomenon. As noted above the elevated levels of thyroid hormone result in suppression of pituitary TSH. Only very rarely does one find a TSH-producing pituitary tumor as a cause of thyrotoxicosis.

The 24 hour radioactive iodine uptake may aid in the diagnosis of some of the atypical causes of thyrotoxicosis, such as subacute (viral) thyroiditis<sup>38</sup> and the newly described "silent" (painless) thyroiditis,<sup>39</sup> both of which are usually transient phenomena. Subacute thyroiditis<sup>38</sup> is thought to be a viral disorder, where the sudden development of a painful and enlarged thyroid gland follows a viral upper respiratory tract infection and is accompanied by an elevated erythrocyte sedimentation rate, a markedly depressed 24 hour radioactive iodine uptake, and normal or only minimally elevated serum antithyroid antibodies. Thyrotoxicosis appears to result from gland injury and subsequent release of thyroid hormone and iodinated precursors. Thus, the PBI measurement may exceed the  $\text{T}_4$  measurement. If a thyroid gland biopsy is performed, granulomas are seen. The clinical course may involve the following sequence: thyrotoxicosis, euthyroidism, hypothyroidism, and then euthyroidism.

This contrasts with the very rare acute (pyogenic) thyroiditis. It also contrasts with Hashimoto's thyroiditis,<sup>37</sup> where usually painless enlargement of the thyroid gland results from a disorder of cellular and humoral autoimmunity. In many cases of Hashimoto's thyroiditis, serum antithyroglobulin and particularly

antimicrosomal antibodies are elevated. Biopsy reveals lymphocytic infiltration and the presence of Ashkanazy cells. Although occasionally early Hashimoto's thyroiditis may present with transient thyrotoxicosis ("Hashitoxicosis"), most patients are initially euthyroid. A significant number may go on to develop permanent hypothyroidism. In this case an early indication of thyroid gland failure is an elevated serum TSH. With TSH stimulation of the failing thyroid gland, there will be a rise in the  $\text{T}_3$  RIA to  $\text{T}_4$  ratio and an exaggerated rise in serum TSH following intravenous TRH administration.

Recently, an additional form of thyrotoxicosis has been described: Silent (painless) thyroiditis.<sup>38</sup> The thyroid gland is nontender and may be enlarged. Otherwise, the clinical course and laboratory findings are nearly identical to those seen in subacute thyroiditis. However, the histology of the thyroid gland is similar to Hashimoto's thyroiditis. Although thyrotoxicosis is usually transient, it may recur. There have also been recent reports that a significant number of patients with silent thyroiditis may ultimately go on to develop permanent thyroid gland abnormalities.

Thyrotoxicosis with a decreased 24 hour radioactive iodine uptake by the thyroid gland also occurs in factitious hyperthyroidism, expansion of the iodine pool by organic or inorganic iodine, and stroma ovarii.<sup>40</sup>

### **Treatment of Hyperthyroidism**

Thyrotoxicosis may be treated by drugs, radioactive iodine, or surgery.<sup>41</sup> In Grave's disease occurring in children and young adults, propylthiouracil or, alternatively, methimazole is favored to block thyroid hormone synthesis. "Spontaneous" remission will occur after one year in approximately 30% of the patients so treated and is more likely in patients with small goiters. In elderly adults, in patients with underlying heart disease or serious systemic illness, and in young adults who have failed two consecutive year-long courses of propylthiouracil or methimazole (or who are adamant in their desire for earlier, more definitive therapy), it is reasonable to treat with radioactive iodine. There is a significant and progressive incidence of eventual hypothyroidism in patients given "treatment" (as opposed to "ablative") doses of I.<sup>131</sup>

Surgery is rarely indicated in Grave's disease. Although surgery is favored by some in uninodular and multinodular toxic goiter, these disorders are probably better treated with radioactive iodine.

The transient thyrotoxicosis of subacute thyroiditis



or silent thyroiditis can usually be symptomatically controlled with the beta blocker propranolol and definitive therapy for thyrotoxicosis will usually not be required. Propranolol may also be useful as the initial form of therapy of thyrotoxicosis when cardiac manifestations are particularly troublesome, regardless of the underlying etiology.

### Conclusion

Recent advances in basic and clinical science have improved our ability to diagnose and treat hyperfunctional disorders of the pituitary and thyroid glands. A careful history and physical examination, appropriate laboratory testing, and useful radiological and nuclear studies remain essential. In many areas improvements in the ability to measure accurately and precisely the

basal levels of hormones have been the diagnostic key. However, in many cases determination of basal hormone levels will not be sufficient and suppression and stimulation tests must be employed. Thus, the central responsibility of the diagnostician of endocrine disorders, like that of the system he/she studies, remains largely unchanged: he/she must act to stimulate that which he/she believes suppressed or deficient; he/she must endeavor to suppress that which he/she thinks excessive.

### Acknowledgments

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# Differential Diagnoses of Short Stature and/or Slow Growth

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Pathologic short stature associated with good health generally arises from a congenital disorder. Most such children have been short all of their lives. Abnormally slow growth associated with good health is usually due to an acquired disease. These children have had normal height in the past and sometime present with normal height despite the slow growth. Particularly important in establishing the underlying diagnosis is a thorough history.

**A**BNORMAL SHORT STATURE and/or slow growth in the young indicates a significant underlying problem. Optimum therapy depends on an accurate diagnosis. The purpose of this paper is to review the differential diagnoses of short stature and of slow growth associated with good general health. We will not consider growth problems associated with serious underlying disease such as cystic fibrosis, chromosomal trisomies, cyanotic congenital heart disease, renal acidosis or inborn errors of metabolism.

## Definitions

We find the following definitions helpful in classifying and studying our patients.

Pathologic short stature: height -4 standard deviations or further below the mean.

Possible pathologic short stature: height -2 to -4 standard deviations below the mean.

Pathologic slow growth: decrease by 1 standard deviation or more in height-length and/or growth.

Possible pathologic slow growth: growth in height less than 5 cm. per year, age 4 to age of puberty.

## Classification

Common causes of short stature are usually congenital and include familial delay in puberty, growth hormone deficiency, Turner's syndrome in girls; intrauterine growth failure, bone dysplasias and benign genetic short stature. Common causes of slow growth are generally acquired and include deprivation, growth hormone deficiency, hypothyroidism, mild

chronic inflammatory disease of the bowel, Cushing's disease-syndrome and drug induced disease.

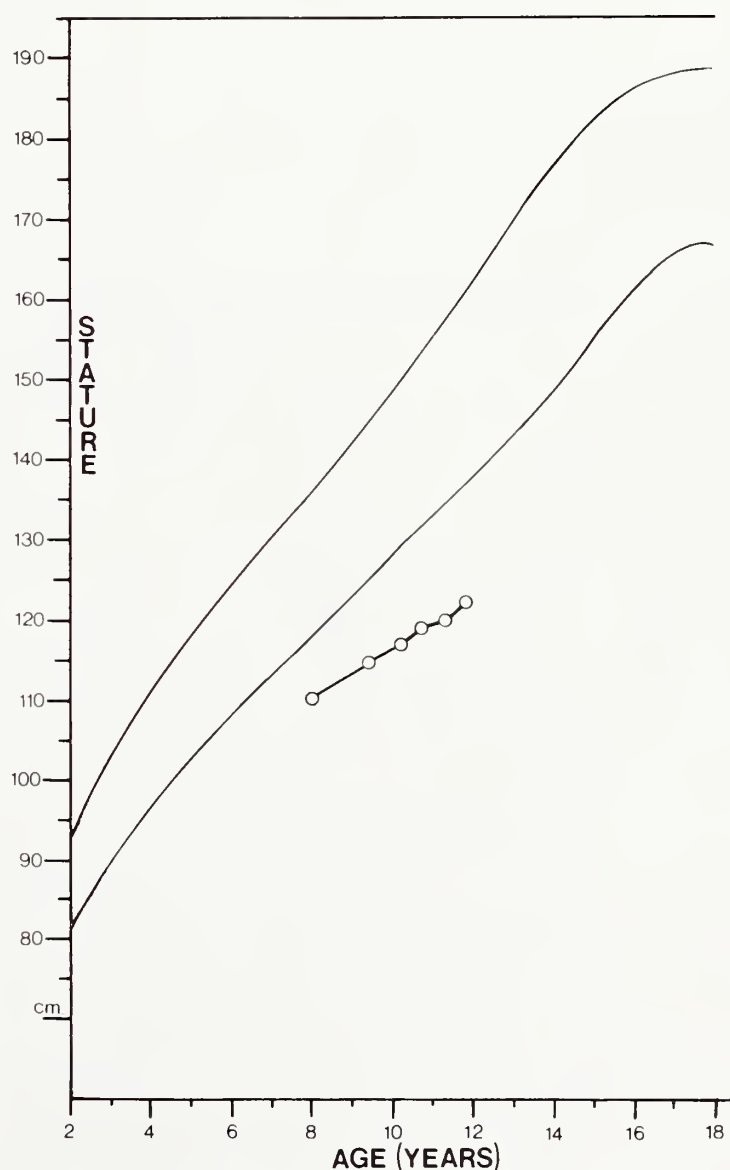


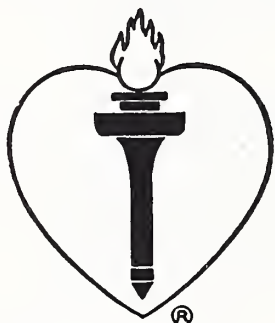
Fig. 1 — Typical growth curve of a child with short stature.

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**CONTRAINDICATIONS** Use in Newborn or Premature Infants: This drug should not be used in newborn or premature infants.

Use in Nursing Mothers: Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Use in Lower Respiratory Disease: Antihistamines should NOT be used to treat lower respiratory tract symptoms including asthma.

Antihistamines are also contraindicated in the following conditions: hypersensitivity to azatadine maleate and other antihistamines of similar chemical structure; monoamine oxidase inhibitor therapy (See DRUG INTERACTIONS Section).

**WARNINGS** Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma; stenosing peptic ulcer; pyloroduodenal obstruction; symptomatic prostatic hypertrophy; bladder neck obstruction.

Use in Children: In infants and children especially, antihistamines in overdosage may cause hallucinations, convulsions, or death.

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

OPTIMINE TABLETS ARE NOT INTENDED FOR USE IN CHILDREN UNDER 12 YEARS OF AGE.

Use in Pregnancy: Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus.

Use with CNS Depressants: Azatadine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).

Use in Activities Requiring Mental Alertness: Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating appliances, machinery, etc.

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

**PRECAUTIONS** Azatadine maleate has an atropine-like action and, therefore, should be used with caution in patients with: a history of bronchial asthma; increased intraocular pressure; hyperthyroidism; cardiovascular disease; hypertension.

**DRUG INTERACTIONS** MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

**ADVERSE REACTIONS** The most frequent adverse reactions are underlined:

*General:* Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat.

*Cardiovascular System:* Hypotension, headache, palpitations, tachycardia, extrasystoles.

*Hematologic System:* Hemolytic anemia, thrombocytopenia, agranulocytosis.

*Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.

*Gastrointestinal System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

*Genitourinary System:* Urinary frequency, difficult urination, urinary retention, early menses.

*Respiratory System:* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

**OVERDOSAGE** Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing; and gastrointestinal symptoms) may also occur.

If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

If vomiting is unsuccessful, gastric lavage is indicated within three hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic and 1/2 isotonic saline is the lavage solution of choice.

Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore are valuable for their action in rapid dilution of bowel content.

Stimulants should not be used.

Vasopressors may be used to treat hypotension.

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### Therapy and Prognosis

We prescribed weak androgens for the short stature and female sex hormones, both estrogen and progesterone, for the development of secondary sexual characteristics. The female sex hormones are given in as low a dose as possible until middle age. Symptomatic therapy is given as indicated for the other problems, e.g., congenital heart disease, learning difficulties.

With anabolic agents the final adult height is generally between 136 cm. and 152 cm. and correlates with the height of biologic parents. With estrogen and progesterone therapy almost all of the girls develop normal secondary sexual characteristics, but of course are sterile.

### *Intrauterine Growth Failure Syndrome*

Intrauterine growth failure occurs in association with a variety of underlying problems: genetic, maternal disease, placental disease or fetal disorder. The mechanism is unknown. By definition full term babies weighing less than 2500 grams have intrauterine growth failure. The natural history is not yet delineated but probably varies depending on the underlying disease. While those with the genetic type seem to have a good prognosis<sup>12</sup> preliminary data suggest that many of the other patients fail to achieve normal adult height and perform less well in school than do their siblings.<sup>13</sup>

### Presenting Manifestations

Now that the syndrome of intrauterine growth failure is quite well known, patients are often identified in the newborn nursery. However, a most frequent presenting complaint is short stature during the first or second decade of life.

### Confirming the Diagnosis

To confirm the diagnosis the clinician establishes that the baby was full term, has or had physical characteristics of the full term rather than a premature baby, i.e., firm ear cartilage, glandular breast tissue, many linear markings on the palms and soles, but significantly lower birth weight than full term siblings. Thus, the diagnosis is a clinical and often historical one. Other causes of short stature may need to be ruled out.

### Therapy and Prognosis

We have no definitive therapy. However, treatment with larger than usual doses of human growth hormone have been helpful in short term studies.<sup>14,15</sup> Long term results are not yet available.

### *Bone Dysplasias*

These disorders are associated with an innate

problem of the cartilage and bone, probably a metabolic one, so that the bones fail to grow normally in length and/or shape. While most of the bone dysplasias are autosomal dominant, a few are transmitted as autosomal recessive. Spontaneous mutations are believed to occur more commonly in the offspring of older fathers. The final adult height varies with the underlying bone dysplasia from 3½ to 5'. Severe bone dysplasias can be associated with impaired hearing and compromised peripheral neurologic functions.

### Presenting Manifestations

Some will look unusual in the newborn nursery because of disproportionately short limbs and generous size head. However, most of the patients present during childhood with disproportionate short stature. The physical findings vary from the typical achondroplastic dwarf with rhizomelic shortening of the extremities, skull large for age or height, frontal bone bossing, exaggerated lumbar lordosis, trident hands, to the child with only pathologic short stature.

### Confirming the Diagnosis

Generally the radiologist confirms the diagnosis from the abnormal shape of the bones, particularly the long bones. Establishing the precise diagnosis from radiographs can be a problem. Several pediatric radiologists have carefully studied a large number of dwarfs and are available to consult on the roentgenograms. With some patients only a bone biopsy interpreted by a specialized pathologist gives the exact diagnosis.

### Therapy and Prognosis

At present no definitive therapy exists for the dwarfing. However, the patients need regular medical evaluation and intervention for possible complications of the dysplasias, e.g., frequent otitis media, weakness of the lower extremities, and cephalopelvic disproportion in the pregnant female.

### *Benign Genetic Short Stature*

Benign genetic short stature implies that a child is short because the parents are short, i.e., within 2 standard deviations of the mean.

### Presenting Complaints

These patients, usually boys, seek help because they are somewhat smaller than their peers. Physical examination including sexual maturation is normal.

### Establishing the Diagnosis

The diagnosis is a clinical one. We measure the parents' weight and plot the data on a growth curve for



18 year olds. The parents' height and patients' height in terms of standard deviations are comparable, e.g., if the patient's height is -2 S.D., one or both of the parents should be approximately at the -2 S.D. level. Further studies are then unnecessary. If the patient's height in standard deviations is significantly less than his parents, further evaluation is indicated. If the patient's height and the parent's height are further than two standard deviations below the mean, the family needs to be studied for genetically controlled disorder, e.g., growth hormone deficiency, bone dysplasia.

#### Therapy and Prognosis

Drug therapy is not indicated.

### Slow Growth

#### Deprivation Syndrome<sup>16</sup>

Deprivation, caloric and/or emotional, slows weight gain and eventually linear growth. In some patients this disorder has occurred in association with transient growth hormone deficiency. Children of all ages can be affected although the entity seems to occur more commonly in infants. While we recognize the disorder more frequently in children from the lower socioeconomic classes, it does occur in upper classes. Generally only one sibling is affected. Often one of the caretakers, not necessarily the biologic parents, is disturbed.

#### Presenting Manifestations

Babies present with failure to gain weight normally. They look impressively scrawny. Older children have severe short stature but tend to be a little plump with unusually full abdomens but wasted buttocks. Developmentally, these patients perform suboptimally.

#### Establishing the Diagnosis

Laboratory studies are of little aid in establishing the diagnosis and should be avoided. The sine qua non is acceleration of weight gain in the young and acceleration of growth in the older, when the patient has a new caretaker, e.g., hospital or foster home. Feedings need to be sufficient for the state of malnutrition and for accelerating growth. For infants a relatively short time is required, about two weeks, for older children several months may be necessary.

#### Therapy Prognosis

If the biologic parent is the psychologically disturbed caretaker, psychotherapy for that parent is essential. If the parent refuses psychotherapy aid can often be obtained through the courts and the patient placed in a new home. When the caretaker is disturbed and is not the biologic parent, a new caretaker must be

located.

The long term prognosis for growth is good. Considerable concern exists, however, for normal intellectual and emotional function.

#### Acquired Growth Hormone Deficiency

Acquired abnormalities of the hypothalamic pituitary area which inhibit growth hormone formation and/or secretion produce growth failure. Examples of abnormalities are hypothalamic pituitary tumors such as craniopharyngiomas, histiocytosis X, severe trauma to the head and therapeutic irradiation of intracranial neoplasms. Other hypothalamic pituitary hormones, vision and personality may be compromised.

#### Presenting Manifestations

Patients present in a variety of ways in part depending on the deficiency, e.g., sudden onset of diabetes insipidus, slowing of growth, sexual infantilism, visual disturbances or combinations of the above.

#### Confirming the Diagnosis

As with congenital idiopathic growth hormone deficiency, acquired growth hormone deficiency is documented by a radioimmuno-assay of growth hormone during two stimulation studies when the patient is euthyroid. Roentgenographic studies and/or biopsies will help diagnose tumors and histiocytosis X.

#### Therapy and Prognosis

Optimum therapy has not been determined for the tumors, (i.e. excision and/or irradiation). For histiocytosis X most oncologists recommend glucocorticoids and antimetabolites. Hormonal therapy must include growth hormone as well as other hormones for which the patient is deficient.

Prognosis for growth is good, but for return of motivation, guarded. Because of the localized invasive nature of some of the tumors, vision may be permanently impaired and the life span shortened.

#### Acquired Hypothyroidism

Normal levels of thyroid hormone are essential for optimal linear growth during extrauterine life. Hence, inadequate amount of thyroid hormones result in slowing of growth. Autoimmune chronic lymphocytic thyroiditis causes most of the acquired hypothyroidism of children and adolescents. Occasionally failure of ectopically placed thyroid tissue, e.g., sublingual is associated with acquired hypothyroidism.

#### Presenting Manifestations

In addition to abnormally slow growth these patients generally have minimal complaints: decreased physi-



cal activity, increased need for sleep and mild constipation. Usually they perform very well in school. Occasionally, pallor and rough, dry skin are marked. Those with ectopically placed thyroid tissue also complain of a mass enlarging, generally at the base of the tongue.

#### Establishing the Diagnosis

Primary hypothyroidism is associated with a low blood thyroxine by radioimmunoassay and an elevation of thyroid stimulating hormone by radioimmunoassay. The presence of antithyroid antibodies, thyroglobulin and/or microsomal, suggests chronic lymphocytic thyroiditis. Via technetium scan, the tongue masses can be identified as thyroid tissue.

#### Therapy and Prognosis

We treat such patients with thyroxine about  $3.5 \pm 0.3 \mu\text{g/kg/daily}$ .<sup>17</sup> For those who prefer we recommend thyroxine one time/week in a dose of  $1.1 \text{ mg/M}^2$ .<sup>18</sup> The clinician should regulate the dose so that the patient is clinically euthyroid and has a normal thyroxine and TSH. Surgical excision of ectopic thyroid tissue is not necessary since the mass will entirely disappear with replacement hormonal therapy.

Prognosis for growth and good health is excellent unless the patient has other autoimmune disease. With replacement therapy some children temporarily experience deterioration in school performance, difficulty getting along, particularly with parents, and loss of scalp hair.

#### *Mild Crohn's Disease*

Crohn's disease, a chronic inflammatory disease of the bowel of unknown etiology but with a strong genetic component, often interferes with growth. The mechanism is not clear but is probably related to suboptimal nutrition.

#### Presenting Manifestations

Growth failure, per se, can be the presenting manifestation of mild "silent" Crohn's disease. Puberty may be delayed as well. On questioning the patient may or may not describe intermittent attacks of abdominal pain and diarrhea.

#### Confirming the Diagnosis

The diagnosis can be confirmed in some from biopsy of the sigmoid mucosa. Roentgenographic studies of the large and/or small bowel with barium are necessary. Radiologists consider the following pathognomonic: in the colon, segmental disease with ulcers, greater than 2 mm. in depth; and fissures perpendicular to the bowel lumen; or in the small bowel: segmental disease with contracted irregular

lumen with loss of mucosal pattern, fissures, and thickened edematous wall.

#### Therapy and Prognosis

Symptomatic therapy with glucocorticoids, salicylazosulfapyridine, hyperalimentation or excision of diseased bowel may be associated with a growth spurt. The long term prognosis for a normal adult stature is variable.<sup>19,20</sup>

#### *Cushing's Disease-syndrome*

Patients with this disorder secrete excess amounts of cortisol and excess amounts of other adrenocortical hormones. As a result they develop unusual physical stigmata. The underlying disease is either due to an adrenal tumor or an abnormality of the hypothalamic-pituitary area with the resultant bilateral adrenal hyperplasia. Since many of the adrenal tumors are malignant mortality can be high. We do not know the natural history of adrenal hyperplasia. However, rare spontaneous remissions have been reported.<sup>21,22</sup>

#### Presenting Manifestations

Although the disease is quite rare in the young, babies as well as teenagers can be affected. Help is usually sought for the increasingly abnormal appearance: obesity, especially of the trunk and face, purplish striae, hypertension, emotional lability and virilization of the external genitalia. Review of growth data invariably shows the pathologically slow growth rate over the past months or years.

#### Confirming the Diagnosis

The diagnosis depends on demonstrating pathologically elevated cortisol secretion, i.e., elevated urinary free cortisol and failure to suppress with low doses of dexamethasone. The response to the administration of larger doses of dexamethasone help to localize the lesion. Suppression with high doses of dexamethasone suggests that the patient has adrenocortical hyperplasia due to an abnormality of the hypothalamic pituitary area, whereas failure to suppress is almost pathognomonic of an adrenocortical tumor.

Invariably patients with Cushing's disease-syndrome have some degree of growth failure and/or short stature. Often children with familial exogenous obesity are referred to physicians because of possible hormonal "imbalance." Children with familial exogenous obesity are almost always taller than average for their age. Hence, this important and simple physical finding negates the need for extensive investigation of possible Cushing's disease-syndrome.

#### Therapy-Prognosis

Surgical excision is the treatment of choice for the



adrenal tumor. While prognosis for the benign adrenal tumor is excellent, the prognosis varies for those that are malignant depending on the degree of malignancy and the extent of the metastases.

For the patient with adrenal hyperplasia we suggest watchful waiting for a spontaneous remission before attempts at additional therapy. Optimal therapy for adrenal hyperplasia has not been determined. However, many recommend total irradiation of the pituitary, O, p'-dichlorodipheyldichloroethane or combinations of those two, adrenalectomy and replacement doses of glucocorticoids and aldosterone. Following successful therapy the signs and symptoms of Cushing's disappear and many children will grow in an accelerated fashion. As a group they achieve a reasonable adult height.<sup>23,24,25,26</sup>

### Iatrogenic

Decreased longitudinal growth has been reported as a complication of several drugs that are used with some frequency in childhood. As early as 1940 it was observed that glucocorticoids inhibited somatic growth in immature animals and shortly thereafter the same effect was noted in children. The most viable of the proposed mechanisms for growth delay are peripheral

antagonism to the action of growth hormone and suppression of somatomedin synthesis or release.<sup>27</sup> Children treated with alternate day glucocorticoids do not demonstrate growth delay. However, the drug must be given in a single morning dose because administration on alternate evenings has been reported to cause inhibition of linear growth.<sup>28,29,30</sup> The diagnosis of growth delay secondary to glucocorticoids is made by history and treatment is by appropriate alterations in steroid dosage after which the child often shows "catch-up" growth.

Neurostimulant drugs including pemoline, methylphenidate, and methamphetamine have been reported to cause poor growth, but this effect has been controversial. The Pediatric Subcommittee of the FDA Psychopharmacologic Drugs Advisory Committee has recently published its conclusions after reviewing the numerous studies regarding neurostimulatory drugs and growth.<sup>31</sup> In the prepubertal child there is a temporary retardation in the rate of weight gain and perhaps also in linear growth, but this has no effect on adult height and weight. This temporary effect on growth seems to be related to drug dosage and the presence or absence of drug "holidays." The diagnosis of drug effect on growth velocity is made by

Table 1

Familial delay in puberty	Observations Helpful in Establishing Cause of Short Stature				Normal Genetic Short Stature
	Congenital Growth Hormone Deficiency	Turner's Syndrome	Intrauterine Growth failure	Bone Dysplasia	
Family history of late puberty	Abnormally low growth hormone levels	Missing sex chromosome	Birth weight after 9 mos. gestation less than 2500 gms.	Disproportionate short stature Abnormal bones on roentgenogram	Patient and at least one parent have height -1 to -2 S.D.
Sexual maturation late but definite	Sexual maturation may or may not occur	Sexual maturation absent or minimal	Sexual maturation normal	Sexual maturation normal	Sexual maturation normal

Table 2

Deprivation	Observations Helpful in Establishing Cause of Growth Failure				Iatrogenic
	Acquired Growth Hormone Deficiency	Cushing's Disease-Syndrome	Acquired Hypothyroidism	Mild Crohn's Disease	
Significant acceleration in weight gain and/or growth during change of patient's environment	Abnormally low growth hormone levels	Elevated free cortisol in 24 hrs. urine specimens	Decreased thyroxine and elevated TSH	Abnormal bowel biopsy and bowel Xrays	History of long term therapy with glucocorticoids
Sexual maturation delayed	Sexual maturation often absent	Sexual maturation early or late	Sexual maturation early or late	Sexual maturation usually late	Sexual maturation often late



history. "Catch-up" growth has been reported after cessation of the drug.

### General Psychologic Support

John Money and his coworkers have studied psychological reactions of patients and parents to growth disorders. Many of the children developed "mascot" syndrome ("known to all, friend to none"), are treated by adults as much younger children and relate to the opposite sex with great difficulty. In addition, patients with Turner's syndrome and some of

those with bone dysplasias have a high incidence of learning defects, particularly as relates to mathematics.<sup>32</sup> We note that for those who fail to mature sexually, particularly the males, the problems are intensified. With appropriate counseling, parents can facilitate normal emotional development and educators can provide appropriate educational programs.

Parents and patients have formed two national organizations who give sensible support to patients and families. We suggest that you refer your patients to them: Little People of America, especially for the adult dwarfs\* and the Human Growth Foundation, especially for younger people.†

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# Parathyroid Disorders

## Pathophysiology, Diagnosis and Treatment

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**Hyperparathyroidism occurs as a primary disorder and as a result of chronic parathyroid stimulation by hypocalcemia. Hypoparathyroidism occurs sporadically, coupled with other endocrine or immune deficiencies, after neck surgery and also on a temporary basis due to hypomagnesemia or after prolonged hypercalcemia.**

**T**HIS REVIEW OF PARATHYROID disorders will focus mainly upon primary hyperparathyroidism and hypoparathyroid states.

Parathyroid hormone (PTH), extracted from parathyroid tissue and possessing biological activity, is an 84 amino acid polypeptide. Biological activity is conferred by the amino terminal one third of the molecule (minimal length 29 amino acids). Although the dominant secreted form of PTH appears to be the intact 84 amino acid peptide, the predominant circulating form of the hormone is a smaller biologically inactive fragment probably comprising the carboxyl terminal 51 amino acids of the peptide chain. This "C terminal fragment" arises from peripheral tissue metabolism of the intact hormone and direct secretion from the parathyroid glands, the relative contributions of each source still being investigated<sup>1</sup>.

The overall secretory tone of the parathyroid glands is set by the concentration of calcium in the extracellular fluid bathing the parathyroid cells with low calcium being a potent stimulus to PTH secretion. Although low calcium has not yet been shown to increase synthesis of PTH, high calcium activates a degradative pathway making less PTH available for secretion<sup>2</sup>. Magnesium, another divalent cation, is required for normal secretion of PTH; low levels of magnesium being associated with decreased parathyroid hormone secretion<sup>3</sup>. Recent interest has focused on catecholamines as potential modulators of PTH secretion. Beta adrenergic agonists have been demonstrated to stimulate PTH secretion in concentrations not different from those found in normal serum<sup>4</sup>.

Many other stimuli of PTH secretion have been noted in experimental systems, but their significance in normal physiology remains unknown. There is a calcium-independent, non-suppressible component of PTH secretion which is probably clinically significant, in that if total parathyroid mass is increased, the non-suppressible component of secretion will result in hyperparathyroidism. This has been demonstrated experimentally by Gittes and Radde who transplanted many parathyroids into individual experimental animals and achieved an animal model of hyperparathyroidism<sup>5</sup>. This model probably best applies to the secondary hyperparathyroidism of chronic renal failure, which has been recently reviewed by one of the authors<sup>6</sup>.

The actions of PTH are noted in Table 1. The principle sites of action are bone and kidney, although receptors for PTH and metabolism of PTH have been noted in the liver. The action of PTH appears to be mediated through two second messengers: (1) PTH causes entry of calcium into cells, (2) PTH causes increased levels of cyclic adenosine monophosphate (cAMP) in its target cells. Although earlier attention had focused on phosphate metabolism, probably the major role of PTH is to maintain calcium homeostasis by mobilizing calcium from bone and conserving calcium at the level of the kidney. As far as has been determined, PTH has no direct effect on intestinal calcium absorption, but may mediate this through

**TABLE 1**  
**Action of PTH**

1. **Bone**  
calcium mobilization  
bone remodeling and formation
2. **Kidney**  
calcium retention (distal tubule)  
phosphate, bicarbonate excretion (proximal tubule)  
1-alpha-hydroxylation of 25-OH vitamin D

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stimulating the renal production of the biologically active form of vitamin D.

### Hyperparathyroidism

Of the causes listed (Table 2), we will discuss only primary hyperparathyroidism (1°HPT). Once considered a rare disorder, recent surveys using serum calcium levels in screening emergency and outpatient hospital visits, have estimated the overall incidence may be as common as 1 person in 1000. Although uncommon in children, the presentation of this disorder is similar to adults. "Kidney stones, abdominal groans, painful bones and mental moans", are less likely to be the initial clinical presentations as is an elevated serum calcium found incidental to a broad screening program. Patients with 1°HPT still commonly present with peptic ulcer disease, nephrolithiasis and systemic arterial hypertension. In the latter case, the hypercalcemia is often first noticed after the patient has been given a thiazide diuretic (see below). Recent evidence has suggested a subpopulation of patients with 1°HPT which has a greater renal sensitivity to PTH<sup>7</sup>, and there may be a physiologic basis for the clinical observation that hyperparathyroid patients developing nephrolithiasis appear to be less likely to develop bone disease. Bone disease is a late finding in 1°HPT and it may be those patients developing stones get medical attention earlier. Clinical descriptions of 1°HPT are available in any standard textbook of medicine, but several less well appreciated points are worth mentioning. Neuromuscular disorders (muscular weakness, decreased vibratory sensations, hyperactive reflexes, cranial nerve abnormalities, abnormal gait, abnormal mental status associated with abnormal nerve conduction and EMG) have been found frequently in patients with primary<sup>8</sup> and secondary<sup>9</sup> hyperparathyroidism. Although it is often written that immobilization of patients with Paget's Disease of bone will result in hypercalcemia, these patients are much more likely to

have 1°HPT as a cause of their increased serum calcium. There is an increased incidence of hyperuricemia and gout in patients with 1°HPT, but calcium pyrophosphate deposition disease (pseudogout) should be watched for, and can occasionally occur in the immediate post-operative period after successful removal of a parathyroid adenoma. Thiazide diuretic therapy often "unmasks" 1°HPT, but it should be noted that any cause of increased bone turnover of calcium can present with hypercalcemia during Thiazide therapy. The mechanism of thiazide induced hypercalcemia is not known, but one explanation is related to increased sodium and calcium reabsorption in the proximal nephron in adaptation to the volume depletion caused by the distal tubular inhibition of sodium reabsorption. The hypercalcemic effect of thiazides may persist for two weeks after stopping the drug. If the patient is determined not to require parathyroid surgery, but needs a diuretic, furosemide should be used as it is not associated with calcium retention.

Rarely, one encounters patients with 1°HPT as part of one of the multiple endocrine neoplasia (MEN) syndromes, and the question is raised as to whether one should screen all patients with 1°HPT for other endocrine tumours. The authors do not recommend this approach unless suggestive symptoms or signs are uncovered by a thorough history and physical examination or the family history is positive for endocrine tumours.

The differential diagnosis of 1°HPT is the differential diagnosis of hypercalcemia (Table 3). Persistently normal serum Ca is almost never seen in 1°HPT although intermittent normocalcemia does occasionally occur. The preoperative workup is aimed at excluding the non-parathyroid causes of hypercalcemia. Although a case can be made for preoperative cervical esophagrams to localize adenomas<sup>10</sup>

**TABLE 2**  
**Hyperparathyroidism**

<b>Primary Hyperparathyroidism</b>
adenoma
hyperplasia
carcinoma
<b>Secondary Hyperparathyroidism</b>
renal insufficiency
rickets/osteomalacia
"renal leak" hypercalciuria
hypocalcemia other than hypoparathyroidism,
e.g., chronic liver disease, malabsorption syndrome
<b>Possible</b>
idiopathic hypercalcemia of infancy
post-spinal injury hypercalcemia

**TABLE 3**  
**Differential Diagnosis of Hypercalcemia**

1. Malignancy
2. 1°HPT
3. Laboratory variation
4. Thiazide diuretics
5. Granulomatous Disease: TB, sarcoid, berylliosis, fungi
6. Thyrotoxicosis
7. Vitamin D excess
8. Addison's Disease
9. Milk-alkali syndrome (especially CaCO<sub>3</sub> antacids)
10. Immobilization (fractures, spine injury)
11. Idiopathic hypercalcemia of infancy
12. Vitamin A toxicity
13. Benign familial hypercalcemia (with hypocalciuria)
14. Subcutaneous fat necrosis in infants



the authors reserve more invasive adenoma-localizing techniques, such as neck vein catheterization and angiography, for patients with previous unsuccessful neck surgery. Thermography, selenomethionine scanning, intraoperative methylene blue, sampling peripheral venous blood for a rise in PTH after squeezing the neck on the side of the adenoma, CT scans of the anterior mediastinum all have their proponents, but have not found "grass roots" support.

The PTH radioimmunoassay deserves further comment as a diagnostic test. The PTH assay is probably the single most useful laboratory test in the diagnosis of hypercalcemia. However, the authors feel that *no hypercalcemic patient should have the decision for or against neck exploration surgery made solely on the basis of the serum PTH*. There is too much overlap between normals and 1°HPT patients in most PTH assay systems to use the PTH assay outside the context of supportive historical, physical and other laboratory findings in making the diagnosis of 1°HPT. Many laboratories apply nomograms or more sophisticated statistical analysis to relate a given level of PTH to serum calcium. Using these techniques a "normal" PTH can be said to have a level "inappropriately high for the degree of hypercalcemia". Although these interpretive techniques are often helpful, some assays do not detect parathyroid suppression well and patients with hypercalcemia of another cause may have PTH values that fall low in the 1°HPT range of the nomogram<sup>11</sup>. The clinician should be wary of the PTH level that is "normal, but inappropriate for the serum calcium", in making the diagnosis of 1°HPT, as a negative neck exploration done by a good parathyroid surgeon is a very lengthy operation.

Some investigators have promoted the use of "nephrogenous" cyclic AMP (40-50% of cAMP excreted in the urine results from PTH action on the kidneys). This test has the theoretical advantage of being a quantitative indicator of biologically active PTH, but published reports demonstrate a considerable overlap between normals and 1°HPT patients. Nephrogenous cAMP requires measurement of serum and urine, but similar information is obtained by expressing urinary cAMP as a function of glomerular filtration (cAMP per 100 ml creatinine clearance)<sup>12</sup>.

Other laboratory aids in the diagnosis deserve comment. Alkaline phosphatase elevation correlates well with significant bone disease but is present in less than one third of cases of 1°HPT. The serum chloride/phosphate ratio combines two frequently seen PTH effects (low serum phosphate and elevated chloride > 102 mEq/ml), but early enthusiasm for this simple manipulation has been dampened by its low

specificity. A recent review of University of Minnesota records suggests nearly all 1°HPT patients, but also a large number of patients with other causes of hypercalcemia, have elevated Cl/P ratios (E. Wong, personal communication). A Cl<sup>-</sup> (mEq/l)/P(mg/dl) ratio greater than 35 still is supportive evidence for 1°HPT and a normal (< 33) ratio should make one suspicious of non-parathyroid causes of hypercalcemia. Although there is a high correlation of elevated levels of serum ionized calcium and hyperparathyroidism, the usefulness of the procedure is highly dependent upon the particular laboratory and is not uniformly reliable. Tests of renal function are non-specific but helpful. Creatinine clearance is also needed for interpretation of other tests. Tubular reabsorption of phosphate [(1-phosphate clearance/creatinine clearance) × 100%] is less than 85% in 1°HPT but may be low in other hypercalcemic states. It should be done on a short timed collection with the patient fasting, and is only useful if renal function is normal. Twenty-four hour urine calcium is very low in the rare entity of "Familial Hypocalciuric Hypercalcemia"<sup>13</sup> and marked hypercalciuria is unusual in 1°HPT.

Subperiosteal bone resorption is seen on Xray in only 10-20% of cases of 1°HPT, but is a fairly specific sign of PTH action. The hand is the most common place to find this sign (especially radial border of middle phalanges), and we do not pursue the matter beyond an Xray of the hands on high resolution film.

The diagnosis of 1°HPT then should be made on the basis of a best fit of the available data (Table 4). The treatment for 1°HPT is surgery. Patients with asymptomatic borderline hypercalcemia may be followed, but most patients do not become better surgical candidates with age. We recommend surgery if a patient has had any of the following: persistent hypercalcemia greater than 0.5 mg/dl above upper limit of normal, nephrolithiasis, peptic ulcer, pancreatitis, change in mentation, an episode of hypercalcemia requiring emergency management, or

**TABLE 4**  
**Investigations in 1°HPT**

1. Repeated hypercalcemia
2. Occult malignancy screen (chest Xray, IVP, serum protein electrophoresis)
3. Serum phosphate
4. Alkaline phosphatase
5. Serum electrolytes (mild hyperchloremic metabolic acidosis)
6. Serum PTH by radioimmunoassay
7. 24 hour urine creatinine clearance, calcium, cAMP
8. Tubular reabsorption of phosphate
9. Xray hands (high resolution film)
10. Thyroid function tests



parathyroid bone disease. Post-operative hypocalcemia is common but transient and can usually be managed with oral calcium supplements. One should be certain these patients are not also hypomagnesemic. The patient in whom surgery is contraindicated can usually be managed uneventfully with oral phosphate, with the dose being titrated to normalize serum calcium. This therapy can be used safely for several years in patients who tolerate it, and the early fears of metastatic calcification may not be borne out. However, very close monitoring of serum levels of calcium and phosphorus plus creatinine clearance to detect progressive deterioration of renal function is imperative in any patient with 1°HPT managed without curative surgery.

### Hypoparathyroid States (Table 5)

Absent or insufficient PTH results in hypocalcemia by at least three mechanisms — decreased calcium mobilization from bone, decreased intestinal calcium absorption due to defective vitamin D metabolism, and renal loss of calcium. Phosphate excretion is decreased and hyperphosphatemia may also aggravate the hypocalcemia. Many cases of hypoparathyroidism (HP) are incomplete, and the serum calcium may occasionally reach near normal levels depending on dietary calcium and phosphate. It is important, in evaluating parathyroid disorders, to obtain a serum phosphate along with the calcium level, because in another major cause of hypocalcemia, osteomalacia, phosphate is usually decreased due to secondary hyperparathyroidism. Hyperphosphatemia with hypocalcemia also occurs in phosphate toxicity, renal failure, rhabdomyolysis and occasionally following cytotoxic therapy. Hypocalcemia is not always symptomatic and is not the only cause of tetany (Table 6). Two common signs of latent tetany are Chvostek's (tapping over the facial nerve produces twitching at the corner of the mouth) and Trousseau's (inflation of a BP cuff on the arm above arterial pressure for two minutes produces carpal spasm). These tests are positive in one-third of hypocalcemic patients. Chvostek's test is positive in 10-25% of normals. Often apparent hypocalcemia can be explained by correcting for a patient's low serum albumin: a useful approximation is that total serum calcium drops 0.8 mg/dl for each gram/dl drop in albumin from normal (about 4.5 gm/dl). If measurements of ionized calcium become more readily available and reproducible they will supplant our present methodology, as it is the unbound ionized calcium which is biologically active.

The PTH radioimmunoassay can be helpful in the differential diagnosis of hypocalcemia because PTH

will be elevated in almost all nonparathyroid causes of hypocalcemia. Pseudohypoparathyroidism (PHP) features elevated levels of PTH due to peripheral tissue resistance to the hormone, but the diagnosis is usually suggested by the unusual physical characteristics of the syndrome. Often PTH is measurable in HP, but is clearly inappropriately low in the face of hypocalcemia.

The signs and symptoms of HP are related to hypocalcemia. Basal ganglion calcification with movement disorders occurs in children and adults with untreated HP or hypocalcemia. Hypoparathyroid children have an increased incidence of subnormal intelligence. Many patients present to us having been treated for epilepsy. Mild papilledema is reported and subcapsular cataract occurs in chronic HP. Hair loss can occur acutely in post-operative HP and patchy alopecia is seen in association with autoimmune HP. Hypocalcemia affects tooth development, and if HP occurs in early childhood, dental aplasia, delayed eruption, hypoplastic enamel and increased caries may be seen. HP is associated with reduced bone turnover, but Xray correlates are inconsistent. Malabsorption occurs, especially in association with idiopathic HP; the mechanism is not known but may be an accompaniment of other disorders of immunity associated with dysfunction of the endocrine system. Hypoparathyroidism is found frequently in association with mucocutaneous candidiasis and may also be found in conjunction with diabetes mellitus, adrenal and thyroid insufficiency and pernicious anemia.

**TABLE 5**  
**Hypoparathyroid States**

1. **Deficient Parathyroid Tissue**
  - a. Postsurgical (rarely post-<sup>131</sup>I therapy)
  - b. Idiopathic, "autoimmune" ± other endocrine deficiencies and candidiasis
  - c. Infiltration — metastases, TB, hemosiderosis, amyloid
  - d. Congenital ± thymus deficiency
2. **Suppressed PTH Secretion**
  - a. Hypomagnesemia
  - b. After correction of chronic hypercalcemia
  - c. Maternal hyperparathyroidism
  - d. Neonatal hypocalcemia (some forms)
3. **Target Tissue Resistance to PTH**
  - a. Pseudohypoparathyroidism (PHP)
  - b. Hypomagnesemia

**TABLE 6**  
**Causes of Tetany**

1. Hypocalcemia
2. Hyperventilation
3. Metabolic alkalosis
4. Hypokalemia
5. Hypomagnesemia



There is no predicatability as to the timing of appearance of these associated disorders whose etiology is uncertain. It is important to be aware of this syndrome since the complexity of its presentation may lead to diagnostic confusion.

Hypocalcemia of the neonate features relative hyperphosphatemia, hypercalcitoninemia and an abnormally low PTH response to hypocalcemia. It is most commonly seen in the setting of prematurity, respiratory distress, birth trauma and infants of diabetic mothers. In the face of a serum calcium less than 7 mg/dl, the presence of symptoms of irritability, seizures or lethargy call for intravenous therapy with 2 ml/kg of 10% calcium gluconate given cautiously over a three to five minute period and follow-up IV therapy with 5-8 ml/kg/day to give approximately 50-75 mg of elemental calcium/kg/day. The serum calcium must be monitored several times a day and the pulse rate observed for bradycardia or other arrhythmias. Parenteral therapy should be discontinued after 48 hours, substituting oral calcium supplementation of the diet with 2-4 grams of calcium gluconate and use of relatively low phosphate containing infant formulas. Persistence of hypocalcemia may indicate primary hypoparathyroidism.

PHP, described in detail by Potts<sup>14</sup>, has characteristic physical abnormalities including short stature, round facies, mental retardation, short metacarpals and soft tissue calcifications as well as decreased response to parenteral PTH as measured by phosphaturia and urinary cAMP. Recently a subgroup has been identified in which the PTH resistance is distal to the activation of adenylate cyclase (parenteral PTH produces no phosphaturia, but stimulates an increase in urinary cAMP). In addition, there are reports of some patients who appear to lack the physical abnormalities characteristic of PHP but who show resistance to administered PTH. Interestingly, hypothyroidism is an occasional finding in PHP.

The diagnosis of HP is suggested by history, physical exam and measurement of serum calcium, phosphate, magnesium, proteins and PTH. The patient's response to PTH (Parathyroid Extract, E. Lilly Co.) should be assessed to determine the nature of the PTH defect<sup>15</sup>.

Treatment of hypocalcemia requires vitamin D and calcium supplementation. Often high doses of vitamin D<sub>2</sub> (ergocalciferol) have been required, and since this vitamin is stored in fat and liver, long term toxicity (hypercalcemia) has been a problem. The dose of

vitamin D<sub>2</sub> used to treat hypocalcemia in hypoparathyroidism is 3000-5000 I.U./kg/day, and to maintain the eucalcemic state, 1000-2000 I.U./kg/day. Calcium supplementation should provide 25-50 mg/kg elemental calcium per day up to a maximum of 1-2 g/day. Dihydroxycholesterol (0.3-1 mg/day in adults) and the recently available 1,25(OH)<sub>2</sub> vitamin D are more rapidly metabolized and toxicity is quickly reversed on stopping the drug. However, these synthetic agents are much more expensive. The dose of 1,25(OH)<sub>2</sub> D<sub>3</sub> is 0.03 to 0.08 µg/kg/day up to an adult dose of 0.25-2 µg/day). In addition, one should reduce the patient's serum phosphate to normal levels using aluminum hydroxide antacids, because the elevated phosphate aggravates the hypocalcemia and increases the likelihood of soft tissue (e.g., vascular and intracerebral) calcifications. Recently, successful treatment of PHP patients has been described with acetazolamide<sup>16</sup> and of HP patients with chlorthalidone<sup>17</sup>. The use of these diuretics for the treatment of patients with disorders of inadequate PTH activity should be reserved for those whose serum calcium levels cannot be maintained by conventional means without frequent episodes of hypercalcemia. The most important aspect of management is frequent laboratory follow-up while establishing an appropriate therapeutic regime, avoiding hypercalcemia and hypophosphatemia.

Hypomagnesemia should always be looked for in assessing patients with hypocalcemia. Magnesium is an important intracellular cation and is necessary for adenylate cyclase activity. Since cAMP generation is required for both PTH secretion and PTH action at the target cell, it is not surprising to find resistance to PTH and defective PTH secretion in hypomagnesemia. This syndrome is most commonly seen in malabsorption, alcoholism and patients on long term intravenous therapy. Treatment with parenteral magnesium (and calcium) quickly restores normocalcemia, but calcium alone gives only transient improvement.

We have made reference to several review articles in the text<sup>1,6,15</sup> and we also would like to call the reader's attention to two other reviews: one of pediatric parathyroid disorders<sup>18</sup>, and another of hypercalcemia<sup>19</sup>.

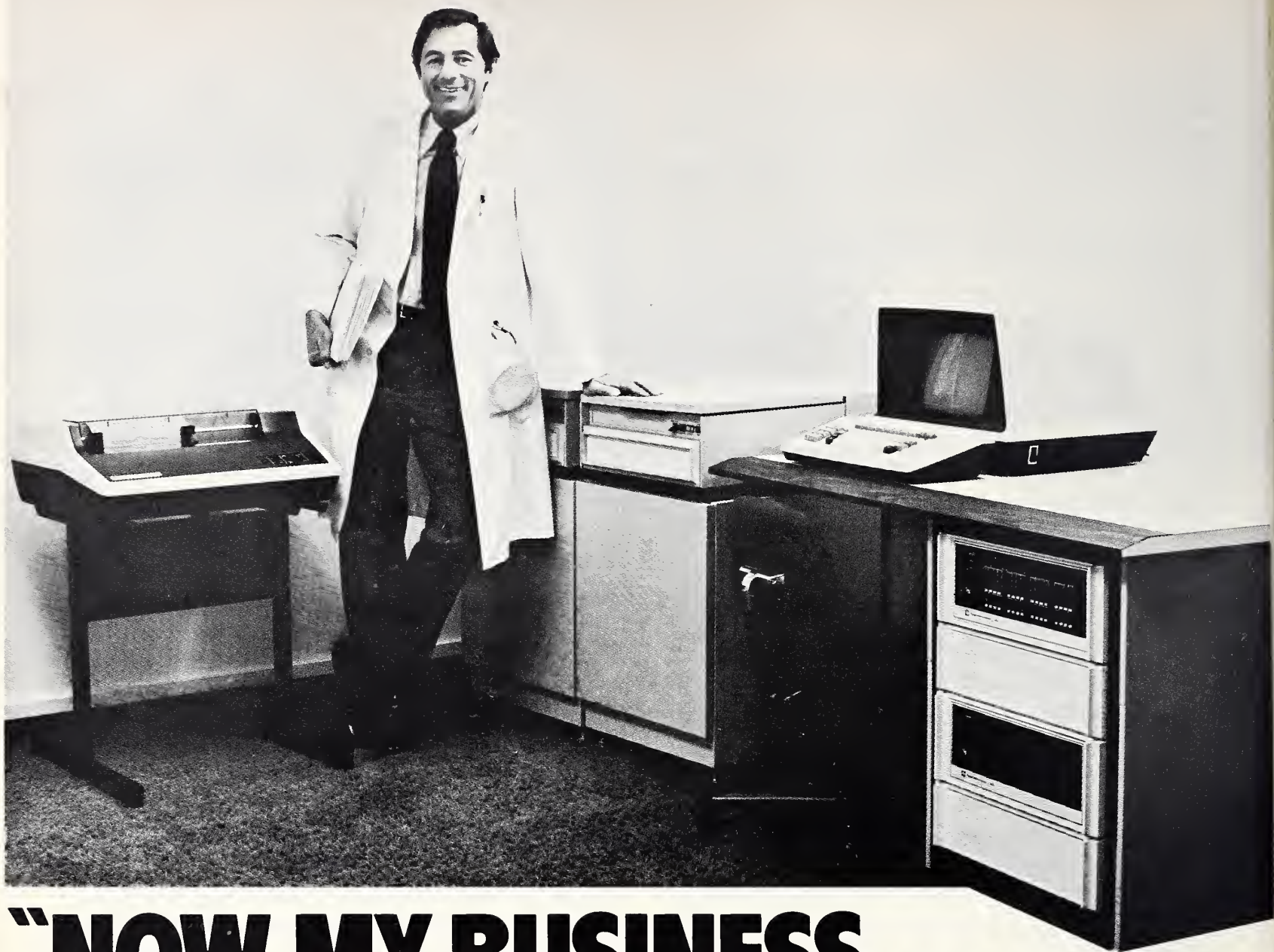
Due to space constraints the authors have not cited all pertinent references. Further references will be provided to the reader upon request.

#### Acknowledgment

The authors wish to acknowledge the excellent secretarial assistance provided by Carol Connelly.

References will be found on page 517.





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# Disorders of Sexual Differentiation

## Ambiguous Genitalia in the Infant A Practical Approach for the Primary Physician

DAVID RAOUL BROWN, M.D.\*

The successful clinical resolution of disorders of sexual differentiation demand a clear understanding of the embryologic and anatomic bases of these anomalies. Appreciation of the underlying genetic, biochemical and physiologic principles of normal sexual development is essential. These conditions must always be considered medical emergencies as there may be potentially lethal underlying metabolic abnormalities and irreversible psychosocial gender adjustment if diagnosis is delayed. A systematic approach to diagnosis and sexual assignment is critical to a clinical understanding and ultimate sexual function. Where a complex decision of gender assignment is present, a multidisciplinary team approach in a secondary or tertiary care center is indicated.

THE PRESENCE of ambiguity of the genitalia, particularly in the newborn infant, should be approached as a medical emergency.<sup>1</sup> Complex and often irreversible psychosocial problems may be averted by rapid and appropriate assignment of gender. Many of these disorders are associated with underlying metabolic abnormalities which may be lethal if not appreciated.

The evaluations of these disorders are delicate and must be systematically approached. Prior to the institution of complex diagnostic procedures the sensitivity of the parents and other family members must be considered. Although rapidity is essential, time must be given initially to establish a clear understanding of the nature of the problem as seen by the clinician. Parents must be spoken with frankly and directly. Physicians must be comfortable and assured in discussing their diagnostic impressions. If there is a lack of familiarity with these disorders, efforts should be made to initiate communication with authorities in this area and the family so informed and supported. Indecision, uncertainty and lack of confidence must be avoided. Regardless of the complexity of the problem and as incomprehensible as it may appear initially, most parents will be reassured by the authoritative approach of a medical specialist and be

able to deal appropriately with the necessary decisions. A precarious encounter initially may often preclude a successful resolution as well as later adjustment for the patient and family. Our approach has been to openly discuss the nature of the disorder as observed on examination and describe all structures, often by direct observation of the patient when appropriate.

Normal sexual anatomy is reviewed and the normal embryology of both sexes is discussed. If a diagnosis is suspected this is shared with the family and possible

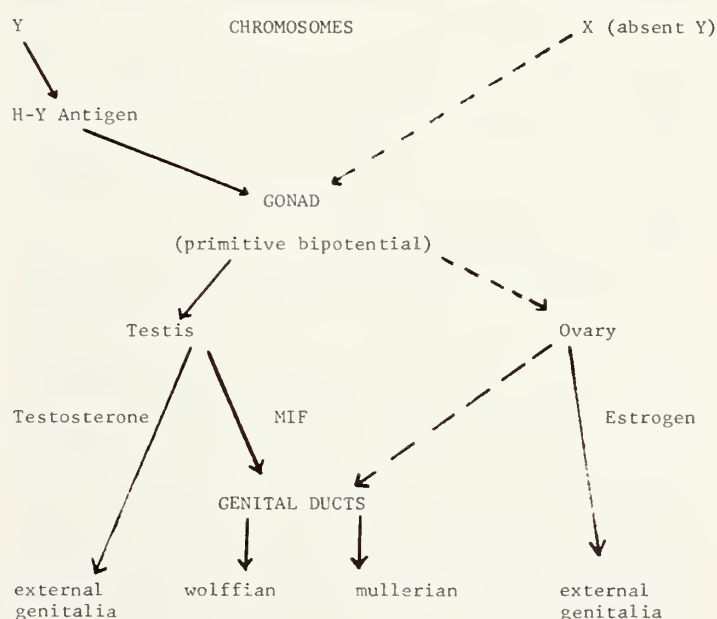


Fig. 1 — Mechanism of Sexual Differentiation.

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developmental mechanisms leading to its appearance are explained. Questions must be encouraged and answered so there is the minimum of uncertainty. Parents are concerned about both the immediate stigma of an "intersex" anomaly and eventual sexual and reproductive function. It is best to avoid ambiguity in the use of sexual terms and homologies between male and female structures and their derivation from common undifferentiated, primordia are to be emphasized.

Immediate consideration must be given to the birth certificate and naming of the child. Submission of legal documents can be deferred and this should be encouraged until a gender assignment is agreed upon. Naming should be withheld until there is an acceptable gender and an equivocal or ambivalent choice should be avoided. The name should be chosen with a specific gender connotation to support the commitment to the ultimate gender identify. Likewise, if a name had already been assigned which is ambivalent or inappropriate to the agreed upon gender it should be changed with the same entrustment. Variations on the original name (e.g. Robert to Roberta or Jacqueline to Jack) or modified spelling (e.g. Gene or Jean or Toni to Tony) as well as equivocal (e.g. Francis or Terry) should be discouraged.

The ultimate decision of gender assignment may be extremely complex, particularly if a role reversal is required. Optimal adjustment is highly correlated with the rapidity of appropriate intervention regardless of parental expectations. Consideration of this selection may be dictated by factors independent of biological circumstances such as genetic constitution, gonadal status or ductal structures. Often mechanical aspects and surgical restrictions must predominate. Where possible parental desires and the ascribed gender should be given optimal consideration. If experience in such decisions is not available, transfer to a secondary or tertiary care center where such expertise is obtainable, should be made.

A team approach is often utilized where a pediatric endocrinologist in concert with the primary physician assumes this responsibility. A multidisciplinary group will include the areas of pediatric surgery, radiology, nursing, support from the chemistry and genetics laboratories and often urology and gynecology. Most important is that all professionals are experienced with these patients and their families. Frequently, religious support is essential both for comfort and support during the initial decision period, but also for guidance

particularly if gonadectomy (i.e. castration) or reversal of gender are in violation of the family's moral tenants. Medicolegal aspects must also be considered and consultation with the forensic establishment may be necessary. The psychological implications of these disorders upon the patient and family vary immensely but must be of primary concern. Psychiatric support may be necessary early in the course of diagnosis and treatment. We have avoided the obligatory inclusion of mental health professionals in the initial assessment of these disorders as it often colors the circumstances as bizarre and unresolvable in the lay person's mind. Psychiatric intervention after the decision of gender assignment is often appropriate and extremely supportive.

### Principles of Sexual Differentiation

The process of mammalian sexual differentiation is a multi-dimensional and remarkable process, the fundamental principles of which are clearly established. The early work of Jost profoundly influenced our thinking in this area and his concepts have proven to apply to the human fetus.<sup>2</sup> The embryonal gonads, sexual ducts, and genital structures are undifferentiated multipotential structures which are influenced by the presence or absence of specific factors to distinguish their characterization. Initiation of the process of differentiation results in a cascade of developmental diversification in which the "female" components appear as a passive manifestation and the "male" components result from a more active process.\*

It is the genetic constitution of the primordial germ cells which commence the sequence of sexual differentiation. The presence of a Y-chromosome facilitates the development of the undifferentiated gonadal ridge into a testis. These gonadal ridges form during the fourth fetal week and by the sixth fetal week contain the primordial germ cells which have migrated from the yolk sac. These germ cells contain the genome from the zygote and if a Y-chromosome is present a cell surface antigen (i.e. H-Y antigen) appears on the gonadal ridge cells and induces the formation of testicular components. In the absence of the Y-chromosome, H-Y antigen does not appear on these cell surfaces and testicular development does not occur. The absence of the Y-chromosome therefore results in the bipotential gonadal proceeding to ovarian differentiation. By the ninth fetal week testicular function has begun. Identifiable ovarian structures may not be apparent until the twentieth fetal week.

The fetal genital ducts are also undifferentiated paired structures. The fetal testis is capable of secreting

\*The author in no way wishes to assume a sexist position and fully appreciates that mammalian sexual differentiation is inherently feminist and will of its own go the way of Eve, but must be led to Adam.



testosterone which acts locally upon this ductal system, and occurs independently on the ipsilateral side. These primitive or mesonephric ducts become organized under the local influence of gonadal testosterone into the wolffian system by the 13th to 15th fetal weeks. In the absence of this local gonadal testosterone this mesonephric duct system degenerates by the tenth to twelfth fetal weeks. The organized wolffian system becomes the primordia for the epididymis, ductus deferens, seminal vesicle and ejaculatory duct.

By the sixth fetal week an additional duct system, the mullerian ducts are also present. In addition to testosterone, the fetal testis also secretes a high molecular weight glycoprotein substance called mullerian duct inhibiting factor (MIF). In contrast to testosterone which is of interstitial Leydig cell origin, MIF is secreted by the fetal Sertoli cell. This substance also acts locally in an ipsilateral fashion and results in the regression of the mullerian duct system. Consequently, in the absence of the fetal testis there will be an absence of MIF and the mullerian ducts will differentiate into fallopian tubes, uterus, cervix and the upper two-thirds of the vagina. This process is likewise passive and the fetal ovary plays no role.

Differentiation of the fetal external genitalia is regulated by the level of serum androgens. During the first eight weeks of fetal life development of the external genital structures is homologous in both sexes, leading to the formation of bipotential genital swellings. Under the influence of testosterone the genital tubercle elongates to form the urethral groove, which by the 11th to 13th weeks is an identifiable penile urethra. Absence of the fetal testis or defective testosterone synthesis will prevent this process and lead to incomplete virilization (i.e. incomplete penile formation and urethral development). However, the fetal adrenal is also capable of synthesizing androgenic compounds so variable degrees of incomplete differentiation may occur depending upon the levels of circulating androgen attained.

Testosterone is not, however, capable of mediating genital differentiation, as the genital tubercle must convert it to dihydrotestosterone (DHT) by the specific enzyme 5-alpha reductase. Specific intracytosol steroid receptors for testosterone and especially DHT must also be present in androgen responsive genital tissues for appropriate utilization to occur. To complete the masculine external genital development the labioscrotal folds, derived from the primordial genital swellings, must fuse to form the scrotum. This

also requires testosterone secretion, conversion and receptor binding. Descent of the testicular gonads occurs as a latter process, probably independent of these mechanisms.

Again differentiation of the external genitalia along female lines is a passive process. As androgen levels are essentially negligible in the absence of a functioning fetal testis minimal differentiation of the genital tubercle occurs. Under the influence of low levels of adrenal androgen it undergoes minimal elongation as a clitoris. The labioscrotal urethral folds do not fuse and form the labia minora. The urethral orifice remains fixed and does not migrate anteriorly in the absence of androgen exposure by the 15th fetal week. Exposure to androgen after this time will not alter the position of the urethral orifice or result in labioscrotal fusion, but the clitoris may hypertrophy in response to significant circulating levels. As the genital swellings also fail to migrate in the absence of androgen stimulation, they fail to fuse as well forming the labia majora. The formation of the lower one-third of the vagina (i.e. introitus) is a consequence of the urethral groove remaining open under these same circumstances. Early exposure to significant androgen levels may likewise modify these relationships.

#### **Systematic Approach to the Infant with Ambiguous Genitalia**

A cardinal rule in the evaluation of these defects is any infant with more than a single genital anomaly is considered a disorder of sexual differentiation until proven otherwise. Often a single anomaly if major is also an indication for evaluation. Nature can be cruel and deceptive as the association of common defects (i.e. cryptorchidism, hyposadius, inguinal hernia) when paired may be the only evidence of a major disorder such as true hermaphroditism. More frequent than not there may be an inverse correlation between what is seen externally and the complexity of variation manifested by the internal gonadal and genital duct structures.

The biologic expression of sexuality is a continuum. "Maleness" and "femaleness" are relative features manifested in varying degrees in each individual. Sexuality may be conveniently classified in categories (Table 1) which in most cases are in conformity and establish the sexual gender identity of the individual. Disorders of sexual differentiation represent gray areas of this spectrum where discordance exists between one or more of these categories. The clinical approach to these patients involves the determination of the child's status with regard to each of these categories and



elucidating the bases of discrepancies utilizing the principles of sexual development as discussed in the previous section.

**TABLE 1**  
**Categories of Sexuality**  
**GENETIC SEX**  
**GONADAL SEX**  
**DUCTAL SEX**  
**HORMONAL SEX**  
**GENITAL SEX**  
**GENDER SEX**

*Genetic sex* refers to the chromosomal constitution, specifically the presence of Y and X chromosomal material and the relative balance of each. The first laboratory study to be done is a buccal smear for determination of the chromatin pattern. Although such studies lack the specificity often required in elucidating these disorders, knowledge of the number of Barr bodies present, provides rapid information essential to directing the clinical evaluation. Peripheral blood karyotyping will give more specific information on the sex chromosome constitution, but it may often be necessary to do genetic analysis on more than one germ layer derived tissue such as fibroblast skin biopsy and eventually gonadal or other genital tissues, particularly if mosaicism of the sex chromosomes is found to exist.

As the presence of Y chromosome in the tissues of genital ridge origin is reflected by the H-Y antigen, determinations of this substance may provide supportive information.

Although the genetic sex need not influence ultimate gender assignment it is often critical in deciding the category of disorder to which the patient belongs and in assisting in decisions regarding the fate of gonadal tissue. An example of the latter is the patient who is chromatin negative and found to have a mosaic form of Turner's syndrome in which a Y-chromosome is also present in the karyotype. The gonadal tissue in such individuals contains undifferentiated embryonal components which lead to eventual malignant degeneration, most commonly as gonadoblastoma or dysgerminoma. The presence of this chromosomal combination is an indication for prophylactic gonadectomy at the time of diagnosis to prevent neoplasia from occurring as well as virilization as a consequence of androgen production by the tumor.<sup>3</sup>

*Gonadal sex* is determined by the presence or absence of H-Y antigen as a consequence of genetic factors, and the local effects of this substance. The eventual development of testicular or ovarian components have already been detailed. Most frequently

gonadal tissue of identical type appears bilaterally. However, dysgenic or fibrotic "streak" gonads may appear on either or both sides. Combinations of both ovaries and testicular components may appear in the same individual, producing the syndrome of true hermaphroditism or mixed gonadal dysgenesis. This may occur with testes, ovary, ovotestis or dysgenic ovary in various combinations on contralateral sides. The essential component in these syndromes is the presence of gonadal tissue of both types in the same patient.<sup>4</sup>

Determination of serum gonadotrophins (LH and FSH) may indicate the absence of gonadal tissue if they are significantly elevated, but provide no information on the type of structures present. Measurements of circulating sex steroids (testosterone, estrone, 17- $\beta$  estradiol and dihydrotestosterone) will give little information in the basal state. Stimulation of the patient with exogenous chorionic gonadotrophin and subsequent sex steroid measurements may assist in elucidating the presence of specific gonadal components if they are adequately differentiated for steroid synthesis and secretion. H-Y antigen determinations may be supportive. Direct visualization by laparoscopy or laparotomy with gonadal biopsy is usually necessary for absolute identification. However, ultrasonography may be of assistance in visualization and localization.

Direct examination of external genitalia tissue is a primary diagnostic modality, but it is not infallible. Palpable structures, particularly if paired, when present in the scrotum or below the internal inguinal ring suggest testes, but ovarian tissue may rarely appear in this location, but do not usually migrate into the labioscrotal folds. Correlation of these findings with chromosomal information is almost always definitive in defining gender.

*Ductal sex* is not evident by external examination, but can frequently be inferred when there is certainty of the genetic and gonadal status of the patient. Radiologic procedures such as voiding cystourethrogram or vaginograms, intravenous pyelograms or abdominal CT scanning may visualize many of these structures, particularly of mullerian duct origin. Cystoscopy may also identify wolffian duct components as well as remnants of mullerian etiology. Abdominal ultrasonography has become the most promising technique for accurate visualization and identification.<sup>5</sup> Often direct visualization by laparoscopy or laparotomy is essential.

The simultaneous presence of recognizable ductal structures of mullerian and wolffian origin may provide important clues to the nature of the disorder.



Suspicion regarding the nature of gonadal tissue present may be derived and definition of possible hermaphroditism or mixed gonadal dysgenesis suggested.

*Hormonal sex* is difficult to investigate in the infant. Provocative stimulation of estrogens and androgens with gonadotrophins may provide some discrimination. It is important to realize that the adrenal cortex is a source of androgen in both sexes. Evaluation of the external genitalia for specific hormonal related effects is probably the most rewarding assessment. Segregation of exogenous from endogenous factors and adrenal from gonadal stimulation is not always possible. However, an appreciation of the normal sequence of fetal differentiation and the timing of these events influencing genital development, as previously described, is extremely helpful in determining when hormonal effects may have intervened, especially when such influences are inappropriate to the patient's assumed gender.

*Genital sex* is the category most amenable to clinical evaluation and is the initiation for suspicion of disordered sexual differentiation as well as the focus for most therapeutic intervention. As these structures are most amenable to direct physical examination, they provide the immediate source of diagnostic assessment. Abnormalities of the external genitalia can be readily documented and clinically described. They are also most clearly available to demonstrate the clinical impressions to parents and health care professionals. Careful documentation of initial and subsequent findings on their examination should be detailed verbally in the medical record. Drawings are often helpful to support such clinical descriptions. Photographs of these structures are extremely useful and are often essential in subsequent surgical decisions involving anatomic correction. Their availability for comparison after reconstructive procedures are of great value in follow-up with families and also deserve medicolegal consideration.

Features to evaluate includes the presence, shape, size, and position of specific genital and gonadal structures. Urinary tract relationships must also be defined. If possible the origin of the urinary stream should be observed and documented. Where this is not possible, visualized orifices should be probed with a soft catheter, under the supervision of an experienced surgical or urological colleague. Associated findings such as genital pigmentation, pubic and genital hair, herniae, precocious maturation or unexplained masses should be evaluated. Other anomalies or systemic findings especially orofacial, cardiovascular, or-

thopedic or abdominal masses may provide clues to associated syndromes. Clinical assessment of blood pressure and hydration status as well as laboratory studies such as serum electrolytes may be essential to defining the presence of an associated metabolic abnormality, especially sodium loss with potassium retention on the basis of adrenocortical insufficiency.

*Gender sex* is the category for which such evaluations are ultimately accountable. It is, however, the most difficult to define in the neonatal period. This refers to the area of psychosocial definition of sexual assignment. Eventually it is the role in which the patient views its sexuality and both relates to and defines its body image. Initially it is the decision to which the medical team guides the family after a consensus arrived at by systematic assessment. It may of course be strongly influenced by parental preconceptions and often irreversible preferences. Ultimate gender identity may however, be appropriately contradictory to the genetic, gonadal, hormonal or genital sex. Most often it will correlate with the genital anatomy and clinically assigned sex. Infrequently gender identity and the assigned sex may eventually become disparate and sexual reassignment may be expedient in later childhood or following puberty.<sup>6</sup>

Money has clearly demonstrated that in the assignment of sex in young infants there is a latitude of choice regarding the psychosocial status as the psychosexual identity is at that time undifferentiated. As further differentiation occurs it is significantly influenced by the postnatal stimulation of rearing much as is language development. Consequently, genetic and hormonal factors do not have an inevitable preordained influence.

When mental health support is needed, it is essential that it be introduced as appropriate for the child's developmental stage and that only those professionals unequivocally experienced with these disorders and their rehabilitation be consulted.

### Clinical Disorders of Sexual Differentiation

#### *Pseudohermaphroditism*

The majority of clinical disorders presenting with ambiguous genitalia will be of the pseudohermaphrodite type (Table 2). These are individuals who possess gonadal tissue appropriate to their genetic constitution, but whose external genitalia are divergent from what is anticipated. Likewise their internal genital duct structures are usually also consistent with their chromosomal and gonadal makeup and the structural defects are restricted to the external genitalia and distal urinary tract.



TABLE 2

## Categories of Disorders of Sexual Differentiation

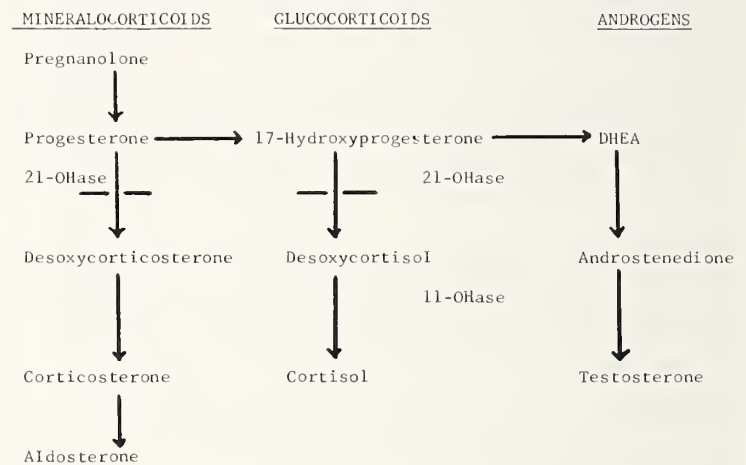
- I. Disorders of gonadal differentiation
  - A. True hermaphroditism
  - B. Mixed gonadal dysgenesis
  - C. Chromosomal disorders
- II. Female pseudohermaphroditism
  - A. Exogenous androgen excess
  - B. Endogenous androgen excess
- III. Male pseudohermaphroditism
  - A. Defects in androgen biosynthesis
    1. isolated defects in testosterone synthesis
      - a. enzyme deficiencies
      - b. Leydig cell hypoplasia or agenesis
    2. combined defects in adrenal and testicular androgen biosynthesis
  - B. End organ unresponsiveness to androgens
    1. receptor defects
    2. Peripheral testosterone conversion enzyme defects
  - C. Estrogen exposure
  - D. Structural anomalies
    1. Hypospadias
    2. Cryptorchidism/anorchia
    3. Microphallus

*Female Pseudohermaphroditism* refers to genetic females with ovarian tissue who appear in a male gender as expressed by their external genitalia. These disorders result from intrauterine exposure to androgenic hormones of endogenous or exogenous origin. The degree of virilization is a function of the magnitude and duration of such exposure and is significantly influenced by the stage of fetal development at which such an insult has occurred.

Exposure to androgenic compounds of non-endogenous origin are usually the result of maternal ingestion of such substances or related steroid compounds which may be converted by the fetus or placenta to androgens. Rarely an androgenic disorder in the mother (i.e. virilizing androgen secreting tumor of the ovary or adrenal or mild adrenal hyperplasia) may be the source of such compounds, but since such conditions are usually associated with infertility, this is a rare situation. A careful history of possible sources of hormone exposure should be obtained. Most frequently the inadvertent continuation of progestin containing oral contraceptives beyond conception is responsible. Unsuccessful attempted abortion by means of high dose progestins has resulted in marked virilization of female infants.

Excessive endogenous androgens are usually the result of metabolic abnormalities. Congenital virilizing adrenal hyperplasia due to enzymatic deficiencies in the glucocorticoid pathway of the fetal adrenal cortex are the most important clinical disorders.

Deficiency of the 21-Hydroxylase enzyme in the pathway of cortisol biosynthesis is the most common of these conditions.<sup>7</sup> In this disorder, diminished levels of the 21-Hydroxylase results in the accumulation of the substrate 17-alpha-hydroxyprogesterone (17-OHP) and deficiencies of desoxycortisol (Figure 2). The

Fig. 2 — Adrenal Cortical Steroidogenesis.<sup>7</sup>

diminished cortisol leads to secondary increases of pituitary ACTH as the result of diminished negative inhibition. 17-OHP is also a precursor in the steroidogenic pathways of adrenocortical androgen synthesis. Under the influence of increased levels of ACTH these pathways are facilitated resulting in the accumulation of adrenal androgens (e.g. DHEA, androstenedione and testosterone). Under the influence of early exposure to these androgens the female external genitalia become virilized (Figures 3 and 4). The increased levels of serum 17-OHP can be readily detected by a specific radioimmunoassay, usually in the first few hours of life, and provide a highly specific diagnostic test for a deficiency of the 21-hydroxylase enzyme.<sup>8</sup> Studies of such patients reveal that the serum level of 17-OHP is directly and quantitatively related to the degree of 21-hydroxylase deficiency. Normal infants show a range of values from 100 to 600 ng/dl clearly discriminating infants with this disorder, demonstrating values of 1400 to 100,000 ng/dl, with values of 30,000 to 40,000 ng/dl most frequently encountered when measured during the third to fifth day of life.<sup>9</sup>

Elevated serum ACTH, DHEA, Androstenedione, and testosterone and urinary levels of pregnantriol and 17-ketosteroids may also demonstrate and support the diagnosis. Recently a specific measurement for quantitative 17-OHP in urine by radioimmunoassay



has become available. This has provided an additional diagnostic methodology, but more importantly is a more discriminating method for evaluating the efficacy of therapy in suppressing endogenous androgen synthesis, than previously available studies.<sup>10</sup>

This disorder is further complicated by additional metabolic abnormalities which may be life threatening. All of these infants have a relative degree of glucocorticoid (i.e. cortisol) deficiency with a diminished cortisol reserve under stress and consequently may be predisposed to acute Addisonian crises manifested by hypotension, hypoglycemia and hydrostatic diarrhea. A 21-hydroxylation step is also required in the mineralocorticoid pathway leading from progesterone to aldosterone. Many of these patients also have a deficiency of the 21-hydroxylase enzyme in this pathway resulting in various degrees of aldosterone deficiency. Such infants may become "salt losers", developing profound hyponatremia and hyperkalemia in the first few days or weeks of life. This may result in marked cardiac arrhythmias and death if not diagnosed and appropriate therapy initiated.

There are at least eleven discrete enzymatic deficiencies in adrenocortical steroidogenesis. In addition to defects in 21-hydroxylation, only those involving the 11-hydroxylase step in cortisol biosynthesis, produce virilization. This later defect is

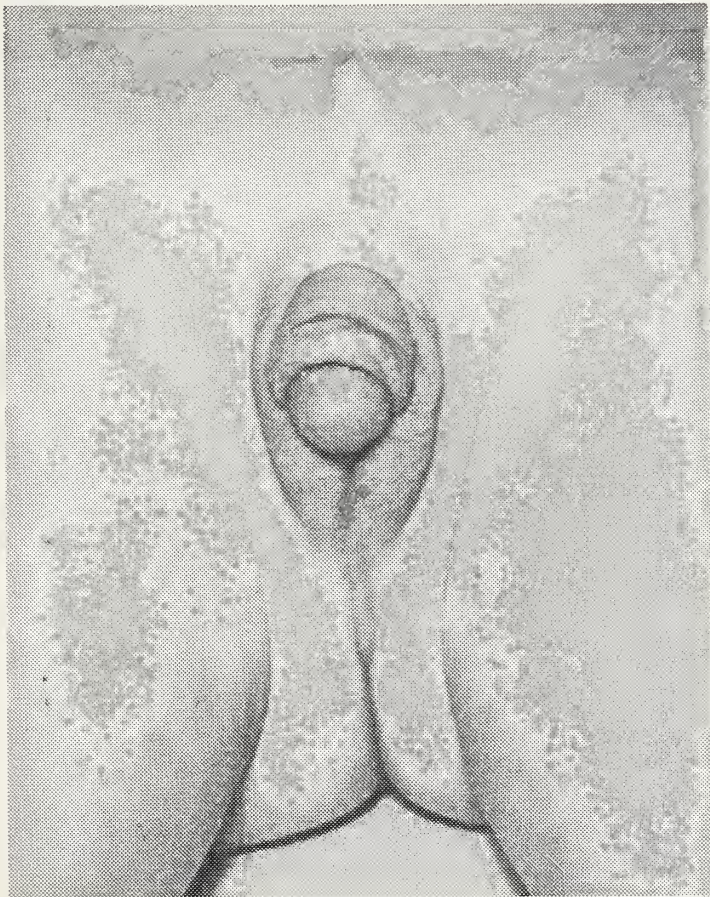


Fig. 3(A) — Female pseudohermaphroditism Dx: 21-hydroxylase deficient congenital virilizing adrenal hyperplasia.



Fig. 3(B) — Female pseudohermaphroditism demonstration of urethral orifice of same patient.



Fig. 4 — Female pseudohermaphroditism Sister of patient (3 a&b) with identical defect.



considerably rarer and is usually associated with hypertension.

As these adrenal enzyme deficiencies are transmitted as autosomal recessive traits, multiple familial occurrence is common. Several hundred cases in siblings are documented.

With early diagnosis, prognosis is excellent. Appropriate cortisol replacement therapy not only corrects its own deficiency, but inhibits endogenous ACTH secretion leading to decreased levels of 17-OHP and thereby diminishes adrenal androgen synthesis with a resulting diminution or arrest of virilization. When necessary, mineralocorticoid replacement corrects the consequences of aldosterone deficiency and sodium loss. Careful clinical and biochemical follow up can establish a near normal growth pattern and normal female puberty, sexual behavior and function and usually fertility may result. Reconstructive surgical procedures may be necessary to reduce the impression of clitoral size (i.e. clitoroplasty), establish an external vaginal orifice or correct associated urinary tract outflow anomalies. Such procedures are not universally indicated and must be appropriately timed and conservatively performed. Again, a team approach and extensive experience are of the essence.

*Male pseudohermaphroditism* refers to genetic males with testicular tissue who appear in a female or

partially ambiguous male gender as expressed by the external genitalia. These disorders result from intrauterine exposure to diminished or absent androgenic hormone effects or rarely estrogen exposure. These conditions result from a more varied but well understood group of underlying mechanisms and are less common than disorders of female pseudohermaphroditism.

These conditions may result from decreased production of androgenic hormones by the male fetus or from an inability to respond to available androgenic hormones or convert precursor to more biologically active forms.

*Defects in androgen biosynthesis* represent enzyme deficiencies in the androgenic pathways similar to those described in adrenocortical hyperplasia. These may be isolated defects in testosterone synthesis limited to the testes or combined defects in adrenal and testicular androgen biosynthesis. Five discrete enzymes are present in the androgen pathways of the testis and adrenal (Table 4). As each of these are determined by autosomal recessive transmission, the resulting syndromes of inadequate virilization are frequently multiple in families. Enzyme deficiencies (e.g. A and B) occur in sequence prior to the formation of progesterone which is a common precursor to androgen and mineralocorticoid synthesis. Consequently, these patients have salt losing tendencies in

**TABLE 3**  
**Homologies of Sexual Structures<sup>11</sup>**

<u>Female</u>	<u>Primordia</u> <u>GONADAL</u> Indifferent Bipotential	<u>Male</u>
Ovary granulosa cells Theca cells ovarian rete	Primordial germinal epithelium	Testis seminiferous tubules Leydig cells Tunica vaginalis
Oogonia Ova	<u>DUCTAL</u> wolffian mullerian	Spermatogonia Sperm
Epoophoron Gartner's ducts		Epididymis Vas deferens seminal vesicles Appendix testis
Fallopian tubes Uterus Upper $\frac{2}{3}$ vagina	<u>GENITALIA</u> Genital tubercle	Penis corpora Glans
Clitoris corpora Glans	Urethral folds	
labia minora labia majora	Labioscrotal swellings	corpus spongiosum scrotum and ventral penis
Bartholin's glands lower $\frac{1}{3}$ vagina	Urogenital sinus	Prostate gland Cowper glands



TABLE 4

**Enzymes in Testosterone Biosynthesis**

- A. 20, 22 — Desmolase  
 B. 3-Betahydroxysteroid dehydrogenase  
 C. 17, 20 — Desmolase  
 D. 17-Alpha-hydroxysteroid dehydrogenase  
 E. 17-Ketosteroid reductase

addition to inadequate virilization, if the defect is present in adrenocortical tissue. Enzyme deficiencies type C, D and E produce only deficient androgen.

Diagnosis of these defects is confirmed by urinary and serum measurements of these steroid intermediaries. Increased levels of precursor substances of the step prior to the enzyme deficiency and low to absent testosterone levels.

Rare patients have been described in which testes are present, but there is a selective absence or diminution of Leydig cell components. Such patients will have absent or low testosterone levels with no rise following chorionic gonadotrophin stimulation. Serum LH will be exclusively elevated, but FSH is normal. Diagnosis is confirmed by testicular biopsy with demonstration of histologic deficiency of Leydig cells.

*End organ unresponsiveness to androgens* represent forms of male pseudohermaphroditism in which testes are present and levels of serum testosterone are normal and frequently elevated.

Testosterone action requires the presence of intracytosol receptors specific for itself as well as for its conversion product DHT (see cover). Classic receptor defects are likely of multiple types resulting from either absent or structurally abnormal hormone binding sites in androgen responsive tissues.<sup>12</sup> The resulting condition is referred to as the testicular feminization syndrome. Estrogen effects are manifested in these patients as the increased levels of available testosterone act as a substrate for estrogen biosynthesis by testicular aromatization. Biopsy of genital tissues will demonstrate qualitative and quantitative changes in testosterone or DHT intracytosol receptors. (Table 5).

Testosterone is converted to dihydrotestosterone by the enzyme 5-alpha reductase present in many

androgen sensitive tissues. This conversion is not necessary for all testosterone peripheral effects, but absence of this enzyme produces syndromes of diminished virilization virtually indistinguishable from receptor defects. Diminished to absent levels of DHT support the diagnosis. Biopsy of androgen responsive tissues (e.g. scrotum, prepuce) will demonstrate deficient 5-alpha reductase enzymatic activity.

TABLE 5

**Male Pseudohermaphroditism (MPH)**

<b>Complete Testicular Feminization Syndrome (T.F.)</b>	<b>Absence of cytoplasmic DHT binding protein (i.e. androgen receptor)</b>
<b>Familial Incomplete MPH (Type I) (Reifenstein syndrome)</b>	<b>DHT Binding intermediate between normals and complete T.F. Quantitative or Qualitative changes in</b> i. Binding affinity ii. Turnover rate (i.e. synthesis) in DHT cytoplasmic binding protein
<b>Incomplete Testicular Feminization Syndrome</b>	
<b>Familial Incomplete MPH (Type II) (Pseudovaginal perineoscrotal hypospadias)</b>	<b>Deficiency of enzyme 5 <math>\alpha</math>-Reductase (T <math>\nrightarrow</math> DHT)</b>

A spectrum of previously described clinical syndromes of male pseudohermaphroditism (i.e. Reifenstein, Lubs, Gilbert-Dreyfus) and familial forms of incomplete masculinization has been clinically reclassified and found to represent receptor, post-receptor binding and conversion enzymes deficiencies which are variations of the classic syndromes described above.<sup>12</sup> An understanding of the basic mechanisms of action and biosynthesis of androgenic steroids has introduced order to the recognition and evaluation of a previously confusing array of patients.

### Therapy

Rapid advances in hormonal replacement therapy and surgical reconstructive procedures have significantly improved the prognosis for these patients. These modalities are worthy of extensive review and will be presented in a follow-up article.

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# Precocious Sexual Development

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Disorders of pubertal development are encountered not infrequently in the pediatric population. With an understanding of the events of puberty, the clinician can logically approach a patient with aberrant pubertal development, arrive at the diagnosis, counsel, and institute appropriate therapy.

**P**UBERTY IS the transition period between childhood and adulthood when maturation of the hypothalamic-pituitary-gonadal axis occurs. During

puberty, the secondary sexual characteristics develop, the pubertal growth spurt takes place, and fertility is achieved. In the male, the onset of puberty is marked by the growth of the testes and scrotum. It occurs normally between 9.5 and 13.5 years of age. Testes

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TABLE 1  
Clinical Staging of Pubertal Development.<sup>11</sup>

Male: Stage	Testes	Pubic Hair
I. (pre-adolescent).	3 ml or less.	Absent.
II.	Slightly enlarged, 3-5 ml.	Sparse. Slightly pigmented. Straight at base of phallus.
III.	Further enlargement, 5-8 ml. Penile and scrotal elongation.	Darker, coarser and curly, extending to scrotum and sparsely on mons pubis.
IV.	Progressive enlargement, 12-20 ml. Penis and scrotum lengthen and widen.	Adult-type hair with further extension to pubis, but less area covered than adult.
V.	Enlarged, 20 ml or greater. Penis and scrotum of adult size and shape.	Adult in type and quantity. Pattern in adult distribution with spread to medial surface of thighs
Female: Stage	Breasts	Pubic Hair
I. (pre-adolescent).	Elevation of papilla only.	Absent.
II.	Stage of breast bud. Elevation of breast and papilla. Enlarged areolar diameter 13 mm.	Sparse. Downy and along labiae.
III.	Enlargement of breast and areola with increasing elevation. Areolar diameter 15-20 mm.	Darker, denser and curlier.
IV.	Secondary mound formed by areolar and papilla, which projects above breast contour.	Fully developed adult type along labia.
V.	Mature state. Projection of papilla only. Recession of areola to general contour of breast. Areolar diameter 30-36 mm.	Adult type. Horizontal pattern of distribution.



greater than 2.5 cm. in longest diameter or 3 ml. in volume can be considered pubertal. Pubic hair appears shortly thereafter. Later, growth of the penis and the pubertal growth spurt occur. In the female, the breast bud is usually the first sign of puberty and develops normally between 8 and 13 years. Later, the pubertal growth spurt takes place and pubic hair appears followed by the menarche. In 10 percent of girls, pubic hair is the first sign of puberty. Tanner has written extensively on the sequence of events of puberty (Figures 1 and 2).<sup>1</sup> His system of pubertal staging describes different levels of pubertal maturation (Table 1).

If a sign or signs of puberty occur before the age of 8 years in the female and 9.5 years in the male, the child should be evaluated for precocious sexual development. Likewise, delayed puberty should be evaluated if the onset of pubertal development has not occurred by 13 years in the female or 13.5 years in the male. Only precocious sexual development will be covered in this review. An understanding of the endocrinology of puberty is essential in approaching a patient with a pubertal disorder.

The factors which influence puberty are seen in Figure 3. Maturation of the hypothalamic-pituitary-gonadal axis depends not only on the integrity of these three organs, but also on the central nervous system (CNS).

The CNS integrates information of the genetic makeup as well as the physical and psychological state of the individual. In general, the timing of the onset of puberty follows that of other family members, particularly those of the same sex. Also, it is well established that disturbances of nutrition and the psyche as well as chronic illness can delay the onset of puberty.

At the appropriate time, the CNS releases its inhibitory influence on the system and sets the gears of puberty into motion. Increasing amounts of luteinizing releasing hormone (LRH) are secreted by the hypothalamus into the hypophyseal portal vessels and transported to the anterior pituitary gland. LRH primes the gonadotrophic cells of the pituitary gland to synthesize and secrete increasing amounts of the gonadotrophins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which in turn stimulate the gonads. Under the influence of FSH and LH, the gonads produce increasing amounts of sex steroids, and the germ cells mature into gametes. The sex steroids stimulate the development of the secondary sexual characteristics which characterize the adult state.

The onset of puberty is heralded by the pulsatile nocturnal secretion of FSH and LH.<sup>2</sup> Prior to the onset of puberty, small amounts of testosterone and estradiol produced by the prepubertal testis and ovary, respectively, are sufficient to produce negative feedback on the prepubertal gonadotrophins, resulting in secretion of only small amounts of FSH and LH. In other words, the sensitivity of this negative feedback system is very high. As puberty progresses, the sensitivity decreases and more FSH and LH is released. A much higher quantity of sex steroid is required to suppress gonadotropin secretion. This decreasing sensitivity to sex steroid feedback is the mechanism through which the CNS controls the onset of puberty.<sup>3</sup>

Other hormones which contribute to pubertal development include growth hormone, thyroxine, and

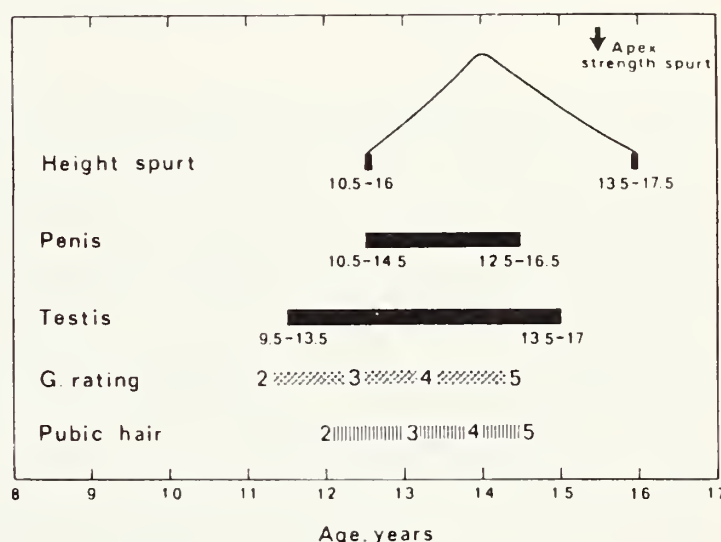


Fig 1 — Diagram of sequence of events at adolescence in boys. An average boy is represented; the range of ages within which each event charted may begin and end is given by the figures placed directly below its start and finish. By permission, W. B. Saunders Company p. 20<sup>1</sup>.

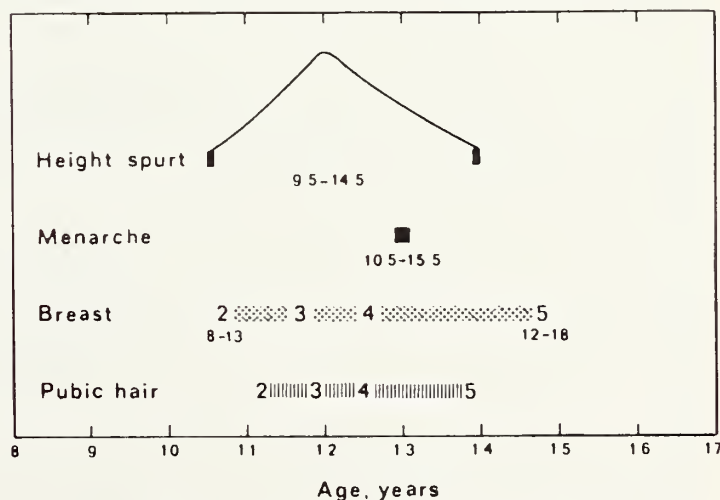


Fig. 2 — Diagram of sequence of events at adolescence in girls. An average girl is represented; the range of ages within which some of the events may occur is given by the figures placed directly below them. By permission, W. B. Saunders Company. p. 31<sup>1</sup>.



the adrenal androgens (Figure 3). The body must achieve a certain somatic maturation which is dependent on these hormones before the onset of puberty can occur. Increasing levels of adrenal androgens can be measured from mid childhood,<sup>4</sup> and appear to precede the nocturnal surges of gonadotropins which signal the onset of puberty. Signs of adrenal androgen secretion include axillary perspiration and odor, facial comedones, oily skin, dandruff, and in females, pubic and axillary hair.

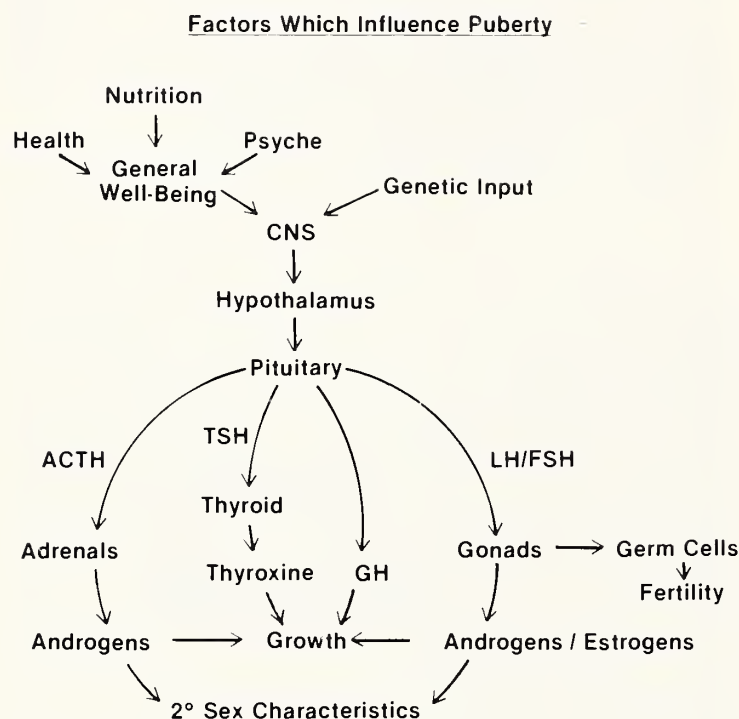


Figure 3

### Precocious Sexual Development

Precocious sexual development may be defined as the onset of a sign or signs of puberty occurring at an age which is statistically younger than the normal range for that sex and ethnic population. If a sign or signs of puberty occur before the age of 8 years in the female and 9.5 years in the male, the child should be evaluated for precocious sexual development. An exception is the female infant born with breast enlargement. She need not be evaluated unless the breast enlargement progresses or persists after one year of age. Twenty percent of girls and 60 percent of boys have a serious organic etiology as the basis for precocious sexual development (Table 2). Therefore, all patients warrant a thorough investigation (Table 3).

Precocious sexual development can be classified into three pathophysiologic categories: true precocious puberty, ectopic chorionic gonadotropin (CG) secret-

ing tumor, and precocious pseudopuberty. True precocious puberty implies early release of inhibition over the hypothalamic-pituitary-gonadal axis, often by an abnormality of the CNS. This initiates the cascade of events resulting in true pubertal development.

True precocious puberty must be differentiated from ectopic CG secreting tumors. Like FSH and LH, CG stimulates gonadal growth and sex steroid secretion with resultant development of secondary sexual

**TABLE 2**  
**Etiologies of Precocious Sexual Development**

- A. True Precocious Puberty**
  1. Idiopathic (diagnosis of exclusion)
  2. Familial
  3. CNS insult or disorder (epilepsy, hydrocephalus, meningitis, encephalitis)
  4. CNS tumor (usually hypothalamic)
  5. McCune — Albright Syndrome
- B. Ectopic Chorionic Gonadotrophin Secreting Tumor (Hypothalamic hamartoma, pinealoma, hepatoblastoma, presacral teratoma, ovarian germ cell tumor)**
- C. Precocious Pseudopuberty**
  1. Male
    - a) Virilizing congenital adrenal hyperplasia
    - b) Adrenal carcinoma
    - c) Testicular tumor (Leydig cell tumor)
    - d) Premature pubarche
    - e) Exogenous androgens
  2. Female
    - a) Ovarian cysts
      - 1) Small — premature thelarche
      - 2) Larger — unsustained or intermittent sexual precocity
    - b) Ovarian tumors
    - c) Exogenous estrogens
    - d) Premature pubarche
- D. Miscellaneous**
  - Primary hypothyroidism.

characteristics. Hypothalamic hamartomas, pinealomas, hepatoblastomas, presacral teratomas and ovarian germ cell tumors are among those which secrete CG in children.<sup>5</sup> They are rare tumors, but are often highly malignant.

Precocious pseudopuberty includes entities in which sex steroids are produced by either the adrenals or gonads independent of hypothalamic-pituitary control. It also includes exogenous steroid administration. The result is development of secondary sexual characteristics mimicing true puberty. Precocious pseudopuberty in the female is usually the result of ovarian cysts, ovarian tumors, or hormone ingestion. The most common cause in the male is virilizing congenital adrenal hyperplasia. Testicular tumors, adrenal tumors and the benign secretion of excess adrenal androgens (premature pubarche or adrenarche) should also be considered.



There are several things in the initial evaluation which should help to place a patient into one of the above categories. It is important to obtain previous growth measurements of the child to determine whether there has been an acceleration of growth which could indicate excessive secretion of sex steroids. A radiograph of the left wrist and hand for skeletal maturation revealing an advanced bone age would substantiate this impression. A history of the age of onset of puberty in other family members may detect a tendency towards precocious sexual development. Detailed history of exogenous steroid exposure must be obtained. The widespread use of oral contraceptives and estrogen creams has led to an increased occurrence of precocious pseudopuberty in girls.

Signs and symptoms of hypothyroidism should be sought since primary hypothyroidism (diagnosed by an elevated level of thyroid stimulating hormone) is a

possible cause of precocious sexual development. A disturbed feedback on the pituitary gland resulting in the excessive secretion of gonadotrophins is thought to be responsible for some cases. Also, a general decrease in metabolic rate may result in decreased clearance of normal quantities of sex steroids potentiating their effects. In contrast to the other entities, short stature and delayed skeletal maturation may be present because of thyroxine deficiency.

The history of a central nervous system insult or disorder is important. It is well recognized that epilepsy, meningitis, encephalitis and hydrocephalus are associated with an increased incidence of true precocious puberty caused by the premature release of inhibition over the hypothalamic-pituitary-gonadal axis. A history of headache, visual disturbance or neurological deficit suggests a CNS (usually hypothalamic) tumor as the cause of true precocious puberty.

**TABLE 3**  
**Evaluation of Precocious Sexual Development**

- A. Initial**
  1. Growth history and radiograph for skeletal maturation
  2. Family history of the onset of puberty
  3. History of exogenous steroid exposure
  4. Signs and symptoms of hypothyroidism. Consider thyroid function studies (including TSH)
  5. History of CNS disorder or insult
  6. Signs or symptoms of CNS tumor (headache, visual disturbance, visual field defect, etc.)
  7. Presence of café au lait spots
  8. (a) Male — Note size of testes and examine for presence of testicular mass. Transilluminate.
  - (b) Female — Bimanual rectal exam to detect ovarian mass. Consider pelvic ultrasound. Examine vaginal mucosa to estimate degree of estrogen secretion.
- B. Further Evaluation Based on Initial Findings**
  1. If true precocious puberty suspected, rule out CNS tumor and ectopic chorionic gonadotropin secreting tumor:
    - (a) Get skull series, ophthalmologic exam and formal visual field testing (if child can cooperate) and consider CAT scan (see text for other diagnostic studies)
    - (b) Get urine pregnancy test as screen to exclude CG secreting tumor and consider serum determination for  $\beta$  subunit of CG
  2. If precocious pseudopuberty suspected
    - (a) Male
      - (1) Testicular mass — surgical exploration indicated
      - (2) No testicular mass and prepubertal size testes — consider adrenal androgen over-production:  
Obtain 24<sup>h</sup> urine for 17-ketosteroids (KS) and pregnanetriol —  
If  $\uparrow$  pregnanetriol +  $\uparrow$  17-KS which suppresses to low dose dexamethasone, then non-salt losing virilizing CAH  
If  $\uparrow$  17-KS not suppressible by dexamethasone, adrenal tumor. Get I.V.P. with tomograms and other studies necessary to localize tumor  
If pubertal 17-KS, premature pubarche
    - (b) Female
      - (1) Ovarian mass — surgical exploration indicated
      - (2) Unsustained or intermittent sexual precocity — close follow-up
      - (3) Premature thelarche — follow-up at regular intervals
      - (4) Pubic hair:  
Obtain plasma testosterone. If elevated, suspect ovarian tumor. Also, obtain 24<sup>h</sup> urine for 17-KS and pregnanetriol and proceed as in 2. a)2) above.



On physical examination, the presence of café au lait spots may direct the physician to a diagnosis. Irregularly shaped café au lait spots (coast of Maine) indicate the McCune-Albright syndrome (polyostotic fibrous dysplasia), a well known cause of true precocious puberty. Oval shaped café au lait spots with regular borders (coast of California) suggest a tumor in the region of the hypothalamus associated with von Recklinghausen's neurofibromatosis. A visual field deficit, decreased visual acuity and optic atrophy further strengthen this impression.

It is important to examine the genitalia in great detail. In the male with unilateral testicular enlargement or mass, a testicular tumor is the presumptive diagnosis. It is often possible to transilluminate a testicular tumor. If both testes are greater than 2.5 cm. in longest diameter or 3 ml. in volume, are of normal consistency, and no masses are present, the patient should be considered to have true precocious puberty.

A careful bimanual rectal exam is necessary in a female, even if it requires sedation or examination under anesthesia. A pelvic mass is detectable in virtually all girls with ovarian tumors. The vaginal mucosa reflects the degree of estrogen secretion. A shiny, pink vaginal mucosa is prepubertal and indicates little estrogen secretion whereas a dusky, thickened vaginal mucosa with a mucousy discharge suggests increased estrogen secretion. A vaginal smear for maturation index and a urocytogram may also indicate the degree of estrogen secretion.

Serum levels of FSH and LH increase with the progression of puberty. Isolated measurements, however, are generally not useful in differentiating between different etiologies of precocious sexual development, because the pulsatile secretion creates wide fluctuations and there is a significant overlap between normal prepubertal and pubertal levels. The gonadotrophin response to an intravenous bolus of synthetic LRH is becoming an important tool in the diagnosis of pubertal disorders.<sup>6,7</sup> In general, there is a characteristic gonadotrophin response to LRH at different stages of puberty. At the present time, LRH is an investigational drug which may become available for general use in the near future. Categorizing precocious sexual development into true precocious puberty, ectopic CG secreting tumor and precocious pseudopuberty helps the clinician organize his approach to the patient and ultimately arrive at a correct diagnosis.

After the initial evaluation, a clinical impression of true precocious puberty necessitates the investigation of an intracranial space occupying lesion. If the patient

has a history of a CNS disorder or previous insult which can explain the condition, the investigation need not be as detailed. Skull radiographs, ophthalmologic exam, and formal visual field testing may show evidence of a brain tumor. Computerized axial tomography<sup>8</sup> and serial tomograms of the sella turcica are important noninvasive radiologic studies that should be considered. Invasive studies such as cerebral arteriography or pneumoencephalography may be necessary to detect smaller central nervous system tumors. A urine pregnancy test may be used to screen for an ectopic CG secreting tumor if one remembers that it is a relatively insensitive test. Serum determination for the  $\beta$  subunit of CG is sensitive and specific and should be obtained if one seriously suspects a CG secreting tumor.

The diagnosis of a brain tumor should result in the consultation of a radiotherapist, neurosurgeon, and oncologist to help determine the most appropriate mode of therapy. A biopsy is often necessary even if the tumor is inoperable. In tumors involving the hypothalamus or pituitary gland, a thorough endocrinologic evaluation should be performed before and after surgery to determine the need for hormone replacement. Patients require a steroid prep preoperatively, and should be monitored closely for the development of diabetes insipidus postoperatively. In a patient without a brain tumor, frequent reevaluation should be performed in order to detect the emergence of an enlarging tumor which had previously been undiagnosed. Treatment of the adverse symptoms of true precocious puberty (the sex drive in males and menses in females) may be accomplished in some patients by the intramuscular administration of medroxyprogesterone acetate 100 mg. biweekly. Unfortunately, it does not totally reverse the development of the secondary sexual characteristics, and does not retard the advancement of growth and skeletal maturation.

The entities which produce precocious pseudopuberty in girls and diagnostic studies will now be considered. The most common entity is premature thelarche; breast development not associated with a vaginal discharge or vaginal bleeding. This is thought to be the result of transient elevations in estradiol secretion by small ovarian cysts.<sup>6</sup> Estradiol levels may be in the prepubertal or early pubertal range, and gonadotrophin response to LRH testing is prepubertal. This is a benign condition which does not result in accelerated growth or skeletal maturation. Patients with premature thelarche should be reevaluated at regular intervals. If pubertal development progresses,



another diagnosis must be sought.

Premature pubarche is not uncommonly seen in girls. This is caused by the secretion of adrenal androgens in quantities which can cause pubic hair growth and slight acceleration of linear growth and skeletal maturation but not virilization. Pubertal levels of urinary 17-ketosteroids and prepubertal plasma testosterone levels are present. This benign condition must be differentiated from androgen producing adrenal and ovarian tumors as well as virilizing congenital adrenal hyperplasia, which are usually associated with virilization and markedly abnormal elevations in urine and plasma androgen levels.

Ovarian tumors must be excluded in girls with precocious pseudopuberty. A rectal exam will detect almost all ovarian tumors. However, unsustained and intermittent sexual precocity<sup>7</sup> produced by an ovarian cyst or recurring cysts are benign conditions which may be difficult to distinguish from an ovarian tumor. All usually present with premature breast enlargement as well as a vaginal discharge which may or may not be bloody. Gonadotrophin response to LRH is suppressed in these conditions and differentiates them from true precocious puberty. Ovarian tumors and cysts may be demonstrable by pelvic ultrasonography,<sup>9</sup> but surgical exploration or laparoscopy may be necessary to exclude an ovarian tumor if other methods are not diagnostic. In general, a functioning ovarian cyst need not be removed if surgical exploration is not required for diagnosis, whereas an ovarian tumor requires salpingo-oophorectomy and exploration to exclude a tumor of the contralateral ovary. Some patients with ovarian tumors require chemotherapy.

The evaluation of precocious pseudopuberty in males is much more straightforward. In a boy with unilateral testicular enlargement and a testicular mass, a tumor must be sought<sup>10</sup> and surgical exploration should be carried out. Chemotherapy may be required. If prepubertal size testes are present, either exogenous steroids or androgens from the adrenal gland should be

considered to be the basis of the precocious sexual development. Premature pubarche has already been mentioned and the clinical findings in boys are similar to those in girls.

Virilizing congenital adrenal hyperplasia is the most common cause of precocious sexual development in boys. The most common form of this condition beyond the neonatal period is the nonsalt losing form, an incomplete deficiency of the 21-hydroxylase enzyme. Elevated 24 hour urine levels of 17-ketosteroids, pregnanetriol and 17- $\alpha$  hydroxyprogesterone with suppression to low dose dexamethasone establishes the diagnosis. An elevated plasma level of 17- $\alpha$  hydroxyprogesterone, the precursor which accumulates before the enzymatic block, is also present. This condition is treated with replacement doses of glucocorticoids and requires close follow-up and the expertise of a pediatric endocrinologist.

Adrenal tumors must also be considered in the differential diagnosis of precocious sexual development in boys. These are often malignant carcinomas which progress rapidly. Elevated levels of 24 hour urinary 17-ketosteroids are usually present and are not suppressed by dexamethasone. Adrenal tumors may be detected by pyelography with tomograms, ultrasound, computerized axial tomography, and radioiodocholesterol scanning. Adrenal vein catheterization with hormone sampling and venography is an invasive procedure which may localize an adrenal tumor. Adrenal tumors should be excised, and patients with adrenal carcinoma should be considered for chemotherapy.

In the management of precocious sexual development, no matter what the cause, it is important to remember that you are dealing with a patient who has the mental and emotional development of a child rather than an adolescent or adult. Therefore, it is important to treat the patient as a child and to counsel family members and other important people in the child's life to do the same.

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# Clinical Management of Delayed Puberty, Impotence and Infertility in Males

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Male hypogonadism is associated with neuroendocrine or testicular disease. Neuroendocrine disorders induced by tumor, dysgenesis or secondary to other disease usually produce hypogonadotropic hypogonadism. Testicular dysfunction produces oligo- or azospermia and/or androgen deficiency associated with hypergonadotropism. Resistance to androgens occurs rarely. Complaints suggesting hypogonadism: delayed puberty, impotence and infertility require evaluation.

**H**UMAN REPRODUCTIVE physiology is a complex interaction of somatic sexual characteristics, gamete production and intricate behavioral patterns. Problems in these areas: undeveloped, underdeveloped or regressing sexual characteristics, infertility, and impotence of organic or psychogenic cause, lead to patients seeking medical advice.

The purpose of this paper is to review the clinical management of these patients. During the past decade there has been a tremendous increase in our knowledge of normal male reproductive physiology. This, in turn, has led to a better understanding of disorders of testicular function and new diagnostic and therapeutic procedures. Therefore, before discussing clinical disorders of delayed puberty, impotence and infertility, the reproductive physiology of men will be briefly reviewed.

## Role of the Central Nervous System<sup>1-3</sup>

The central nervous system (CNS) integrates environmental stimuli, behavior and neuroendocrine control of androgen production. Androgens, in turn, modulate behavior.<sup>4</sup> An intact hypothalamus and pituitary are needed for sexual function. Luteinizing hormone releasing hormone (LHRH) is produced in neurosecretory cells of the hypothalamus and released into a portal vascular channel communicating with the anterior pituitary. The synthesis and release of LHRH is presumably modulated by synapsis with cells from higher centers.

At the pituitary, LHRH acts by binding to surface receptors of both luteinizing hormone (LH) and

follicle-stimulating hormone (FSH) producing cells. LHRH stimulates both synthesis and release of LH and FSH.

Another pituitary hormone important to male reproduction is prolactin. In lower animals, prolactin plays a synergistic role with gonadotropins in the testes and with gonadal steroids in accessory reproductive organs. To date, the major clinical significance of prolactin in men has been a paradoxical suppressive role of high prolactin concentrations on gonadal function.<sup>5</sup>

## Testicular Factors, the Leydig Cell<sup>2</sup>

The expression of secondary sexual characteristics is primarily regulated by steroids secreted by the Leydig cell. Testosterone is the major androgen secreted by the Leydig cell. The effects of testosterone on secondary sexual characteristics are mediated by the conversion of testosterone to dihydrotestosterone in many androgen-sensitive tissues. As with other steroids, androgens are bound to a cytoplasmic receptor and translocation of the receptor steroid complex into the nucleus is necessary for action. Congenital absence of this receptor or inability to convert testosterone to dihydrotestosterone results in the testicular feminization syndrome. In addition to androgens, the testes produce small quantities of estrogens and some testosterone is converted to estrogen peripherally. The role of these estrogens is not known.<sup>6</sup>

Synthesis and secretion of steroid hormones by the Leydig cell is controlled primarily by LH, although FSH and prolactin may have synergistic roles. LH acts on the Leydig cell in a manner similar to other tropic hormones. It binds to a membrane receptor and induces

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the formation of cAMP. The placental hormone, human chorionic gonadotropin, (hCG), also has a similar action and is probably responsible for the production of testosterone in utero.

### **Testicular Factors, the Seminiferous Tubules<sup>2,7</sup>**

Sperm are produced in the seminiferous tubules, which make up the majority of the volume of the testes. Spermatogenesis is, of course, necessary for fertility but plays no role in libido or secondary sexual characteristics. Spermatogenesis is primarily under the control of FSH. FSH binds to a membrane fraction of the testes and stimulates cAMP production. LH-stimulated testosterone, in locally high concentrations, is necessary for sperm maturation. LH and prolactin may also have direct effects on spermatogenesis.

### **Feedback Control<sup>1,2,7</sup>**

As a general rule, endocrine systems are controlled by negative feedback. This holds true for the gonadotropins, LH and FSH. Leydig cell failure or castration results in a fall in serum testosterone and a rise in serum LH. The administration of testosterone by infusion in physiologic quantities will suppress LH. Estrogens also suppress LH.

The feedback control of FSH is not as clear. Pharmacologic doses of estrogens and testosterone will suppress FSH. However, men with azospermia and normal Leydig cell function have selective elevations of FSH. Therefore, some product of the seminiferous tubule must feed back on the pituitary or hypothalamus. This putative substance has been given the name, "inhibin".

The gonadal steroids exert their feedback control both at the hypothalamus and pituitary. Thus, LHRH stimulation of gonadotropins is suppressed by pharmacologic doses of gonadal steroids. Circulating gonadal steroids are largely bound to a carrier protein and, as with other non-peptide hormones, the unbound hormone concentration appears to correlate with feedback.

We shall now turn our attention to the three common problems that patients bring to their physicians: delayed onset of puberty, impotence, and infertility.

### **Clinical Assessment of Delayed Puberty<sup>7-9</sup>**

A useful definition of delayed puberty is no physical manifestations of sexual maturation in a boy at an age which is 2.5 standard deviations above the mean age of onset puberty. Since increase in testicular size is the first manifestation of puberty, a practical definition is testicular length less than 2.5 cm in boys over fourteen

years of age. Testicular size can be measured more accurately by comparing the testes to ellipsoids of known volume (orchidometer). A value of less than 3.4 cm<sup>3</sup> in boys over fourteen years of age is abnormal. We believe all boys who meet this criteria should be evaluated. Evaluation should determine whether the child has constitutional delay, gonadotropin deficiency or hypergonadotropic hypogonadism (Table 1).

**TABLE 1**

#### **Classification of Delayed Puberty**

1. Constitutional delay in growth and development
2. Hypogonadotropic hypogonadism
  - A. CNS disorders
    - extracellular tumors — craniopharyngiomas and germinomas
    - pituitary adenomas — functioning and non-functioning
    - congenital malformations
    - granulomas — histiocytosis X, sarcoid, tuberculosis
    - post-traumatic panhypopituitarism.
  - B. Severe illness
  - C. Idiopathic and genetic forms of pituitary insufficiency
  - D. Isolated gonadotropin deficiency
    - Kallman's syndrome
    - Isolated LH deficiency
  - E. Miscellaneous
    - Prader-Willi syndrome
    - Lawrence-Moon Biedl syndrome
3. Hypergonadotropic hypogonadism
  - A. Klinefelter's syndrome
  - B. Anorchia and cryptorchidism.

The history should include information on the growth curve of the child and every effort should be made to obtain information on the age of onset of puberty and height of male relatives. Children with constitutional delay are usually short (-2SD) and have been so for years. Family history usually reveals that their male relatives were also late in reaching puberty. At present, there is no laboratory test which is useful in separating constitutional delay from gonadotropin deficiency.

The history should also search carefully for evidence of other tropic hormone deficiencies and diabetes insipidus. The most common CNS tumors which cause gonadotropin deficiency and delayed puberty in children are craniopharyngiomas and are usually accompanied by headaches, visual disturbances and evidence of other tropic hormone deficiencies. Pituitary tumors, although rare in this age group, can cause delayed puberty. Tumors delay puberty either by blocking LHRH from reaching the pituitary or by displacing gonadotropin cells in the pituitary. Rarely,



hyperfunction such as in Cushing's disease or prolactin hypersecretion may cause delayed puberty by suppressing gonadotrophin release.<sup>9</sup>

Midline congenital malformations may also cause hypogonadotropic hypogonadism and may be suggested by the presence of optic atrophy, cleft palate or cleft lip. Severe head trauma may sever the pituitary stalk and cause hypopituitarism and should be carefully sought for in the history.<sup>10,11</sup> Children with idiopathic and genetic forms of multiple pituitary hormone deficiencies usually present with short stature at a much earlier age, and the presence of severe chronic disease is usually clearly evident.

The most common form of isolated gonadotropin deficiency is associated with agenesis or hypogenesis of the olfactory lobes which causes LHRH deficiency (Kallman's syndrome). In contrast to children with CNS lesions and constitutional delays, boys with isolated gonadotropin deficiency are usually of appropriate height for their age. Since affected individuals usually do not notice their impaired olfaction, careful objective testing using graded dilutions of pure scents (not irritants) is necessary when evaluating delayed puberty. Rarely, isolated LH deficiencies may occur with normal olfaction.

Rare causes of hypogonadotropic hypogonadism resulting in delayed puberty are the Prader Willi syndrome (hyperphagia, gynecomastia, small hands and mental retardation) and the Lawrence-Moon Biedl syndrome (polydactyly, obesity, mental retardation and retinitis pigmentosa).

Delayed puberty due to primary testicular disorders are accompanied by increased gonadotropin levels. The most common of these is Klinefelter's syndrome. Klinefelter's syndrome is caused by a genetic defect resulting from an extra X chromosome (XXY). It occurs in one out of every 500 males. These children usually present with some degree of sexual maturation, but a failure to complete sexual maturation. Other genetic abnormalities include XY/XXY, XX YY and XXXY karyotypes. The XXXXY karyotype is a specific syndrome characterized by severe mental deficiency, skeletal abnormalities and hypoplastic external genitalia. Diagnosis of genetic primary testicular disorders is made by karyotype and in pubertal ages, elevated gonadotropins.

The lack of palpable testes in a male with XY karyotype indicates cryptorchidism or anorchia. Stimulation with 5000 units of HCG over five days will result in increased serum testosterone if Leydig cells are present. Most cryptorchid testes will descend spontaneously by the late prepubertal period and probably represent "retractile testes" rather than true

cryptorchidism. Failure of the testes to descend normally by the late prepubertal period probably indicates a primary testicular defect. We recommend waiting to see if normal descent will occur before resorting to orchiopexy. Abdominal testes have a slightly increased risk of malignancy but this continues even if the testes are surgically placed in the scrotum.

Androgen deficiency *in utero* results in male pseudohermaphroditism, a condition in which the genetic and gonadal sex are male but the external genitalia are female or ambiguous. *In utero* androgen deficiency can result from 1) enzymatic defects in testosterone synthesis, 2) defects in intracellular conversion of testosterone to dihydrotestosterone, and 3) androgen receptor defects. Once a normal XY Karyotype is established with certainty, the presence of female or ambiguous genitalia would be evaluated with specific enzyme, steroid metabolite and receptor assays.

### Laboratory Evaluation of Delayed Puberty

The minimal laboratory examination of delayed puberty includes: serum LH and testosterone on at least two occasions, serum prolactin, T<sub>4</sub>, lateral skull x-ray, bone age and buccal smear. Depending on findings, stimulatory tests for other tropic hormone deficiencies and further CNS evaluation including CAT scan may be indicated.

### Treatment of Delayed Puberty

Treatment of delayed puberty is dependent on the diagnosis and nature of the disorder. Numerous hormonal regimens for treating constitutional delay have been recommended but since these all result in closure of the epiphysial plate and may limit ultimate height, we recommend watchful waiting. It is helpful to reassure the parents that late-maturing boys reach the same level of achievement in later life as their normal-maturing peers.<sup>13</sup> Treatment of hypogonadotropism is directed first at the cause of the hypogonadism and second at replacing other tropic hormone deficiencies, and finally, at inducing secondary sexual characteristics. Patients with hyperprolactinemia may respond to bromocryptine treatment and successful treatment of Cushing's syndrome results in normal puberty. The remaining patients with hypogonadotropism will all eventually require hormonal therapy to induce secondary sexual characteristics, but it is important not to begin too soon if there is associated short stature. Testosterone enanthate or cypionate, 200 mgm i.m. every two to three weeks will cause a pubertal growth spurt and development of sexual characteristics. Oral methyl testosterone should



not be used because of the danger of liver damage. There may be some theoretical advantage to treating with hCG or even LHRH to induce puberty but these treatments are expensive and require multiple injections so are best considered research procedures for the present.

When these children reach adulthood and marry, it is possible to temporarily induce spermatogenesis and fertility using a course of hCG followed by human menopausal gonadotropins (Pergonal), provided there are no social or genetic contraindications. Children with primary testicular disorders and normal stature may be started on testosterone therapy immediately but it may not be possible to induce spermatogenesis in these patients.

Evaluation of Impotence<sup>7,9,14-16</sup>

Impotence is failure to achieve or maintain an erection. Evaluation should determine if the cause is organic due to androgen deficiency or other causes, or psychogenic. The most frequent cause is psychogenic (Table 2).

TABLE 2  
Classification of Impotence

- 1. Androgen deficiency
  - A. Hypogonadotropic
    - C.N.S. lesions
    - Cushing's syndrome
  - B. Hypergonadotropic
    - Klinefelter's syndrome
    - physical injury
    - post-infectious
    - hematichromatosis
    - renal disease
    - myotonic dystrophy
- 2. Other
  - A. Drugs
    - alcohol
    - phenothiazines
    - anti-hypertensives
  - B. Autonomic and vascular dysfunction
- 3. Psychogenic.

The physician must elicit a frank discussion of sexual practices from his patient. Interest in sex, frequency of erections, frequency of intercourse and specific sexual techniques must be recorded. If the patient's impotence is not total, information concerning time and situations associated with erections as well as failure to achieve an erection is important. Incomplete impotence is frequently psychogenic. A careful drug history and endocrine review of systems must be obtained. Androgen deficiency is accompanied by a decline in facial hair and premature facial wrinkling. Small testes may also indicate androgen deficiency. A diameter of less than 4 cm is definitely

abnormal. The laboratory will confirm the presence of hypogonadism. Low serum testosterone with inappropriately low gonadotropin concentrations indicates hypogonadotropic hypogonadism while elevated gonadotropins indicate primary testicular failure.

The CNS causes of hypogonadotropic hypogonadism are essentially the same as those causing delayed puberty. Pituitary adenomas are much more frequent, however, and craniopharyngiomas, rare. One-third of the pituitary adenomas may be autonomously secreting prolactin and causing hypogonadism by this mechanism rather than by a mass effect. Carotid aneurysm is an additional rare cause of hypogonadism in the older age group.

Hypergonadotropic hypogonadism is much more common in the post-pubertal age group. Klinefelter's syndrome may present in the adult age group as either impotence or infertility. Physical injury, usually due to bilateral hernia repair may cause hypogonadism. Bilateral orchitis, especially due to mumps occurring after puberty, may cause hypogonadism and should be sought for in the history. Hemachromatosis is usually associated with small testes and hypergonadotropism but a second defect in the pituitary may be present. Severe renal disease is usually associated with increased gonadotropin levels.

Differentiating nonandrogen-deficient organic causes from psychogenic impotence is by exclusion. The effects of alcohol on sexual function are well known. In addition, alcoholic cirrhosis can cause hypogonadism due to a double defect in the pituitary and gonads. Impotence due to psychoactive drugs, centrally acting antihypertensives and spironolactone is a growing problem. The incidence of partial impotence due to these drugs is much greater than published figures would indicate. Vascular lesions to the blood supply and autonomic denervation of the genitalia can cause impotence, particularly in the diabetic and following prostate surgery. Diabetes is the most frequent cause of nonpsychogenic impotence.

Treatment of Impotence

Treatment of androgen deficiencies is the same as outlined for delayed puberty and the results are generally satisfactory. Counseling of the patient and his partner may help. Drug-induced impotence is usually partial and a frank discussion of successful sexual techniques and suggestions (permission) to maximize erotic stimulation may be helpful. Every effort to reassure the patient and reduce anxiety over his performance should be made. Psychogenic impotence should be treated in the same way. If the



physician is not comfortable dealing with this problem or initial counseling efforts fail, both partners should be referred to someone skilled in sex therapy.

For the patient with autonomic denervation or vascular lesions, the physician should consider referral for implantation of a penile prosthesis. Patients with longstanding psychogenic and other nonandrogen-deficient causes of impotence may also be considered for referral after adequate testing and all other forms of treatment have been attempted.

### Evaluation of Infertility<sup>7,12</sup>

All of the conditions causing impotence can cause infertility and should be sought for. The hypergonadotropic causes of impotence discussed may also affect spermatogenesis to a greater degree than Leydig cell function and present as primary oligo- or azospermia.

In addition, there are a group of non-endocrine conditions which may cause infertility (Table 3). The Sertoli-cell-only syndrome is a relatively rare condition characterized by slightly decreased testicular size and increased FSH concentrations. Its etiology is unknown, but most likely represents a congenital defect in spermatogenesis. Diagnosis is confirmed by

**TABLE 3**

#### Classification of Infertility

1. Androgen deficiency
2. Adult seminiferous tubule failure
3. Sertoli-cell-only syndrome
4. Mechanical obstruction to sperm transport
5. Retrograde ejaculation
6. Varicocele.

testicular biopsy.

Mechanical obstruction to the vas deferens, either congenital or acquired due to gonoccal or granulomatous disease, will cause azospermia. All patients with azospermia and normal FSH and LH levels should have a testicular biopsy. The diagnosis is confirmed by the presence of normal spermatogenesis on biopsy.

Autonomic dysfunction may cause retrograde ejaculation into the bladder. This frequently occurs in diabetics. Phenothiazines may also cause retrograde ejaculation. The diagnosis is confirmed by the history of failure to ejaculate with orgasm and cloudy urine following intercourse.

Another cause of infertility is unilateral varicocele. In addition to oligo- or azospermia, sperm motility is depressed and increased numbers of tapered sperm are seen. The mechanism is unknown.

### Treatment of Infertility

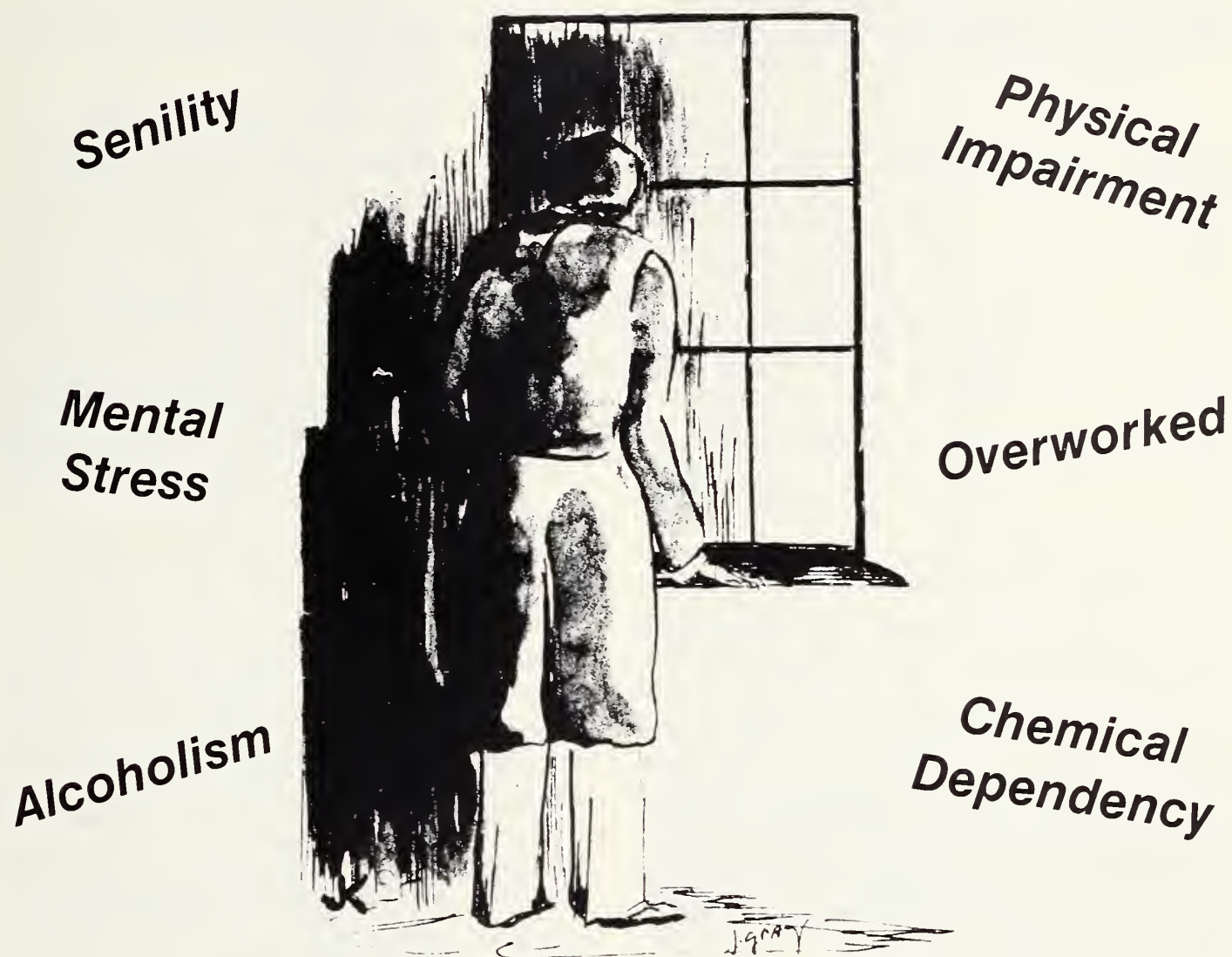
Retrograde ejaculation may respond to the anticholinergic effects of Oranade<sup>®</sup> bid. Two-thirds of men will show improved spermatogenesis following varicocelectomy. Procedures to repair the vas deferens may be attempted but are frequently disappointing. For the majority of patients with a primary defect in spermatogenesis, there is little to offer in rational therapy. Testosterone rebound therapy may be attempted.<sup>7,17</sup> Our understanding of the complexities of spermatogenesis is progressing. This will undoubtedly lead to a more specific classification of disorders of spermatogenesis and specific therapies for infertility in the future.

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(Continued to Page 542)

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(diethylpropion hydrochloride NF)

**Tenuate Dospan** <sup>®</sup>

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine<sup>®</sup>) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

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# Current Approach to the Diagnosis and Management of Pheochromocytoma

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The key to pheochromocytoma diagnosis is the signs and symptoms almost always due to excessive production and release of catecholamines. Other clues include cholelithiasis, neurofibromatosis, and multiple endocrine neoplasias. Abnormalities in catecholamine biochemistry confirm the diagnosis, and computed tomography may localize the tumor. Although rare, pheochromocytoma should be given serious consideration in all cases of hypertension.

IT IS MOST APPROPRIATE to include pheochromocytoma in this issue of MINNESOTA MEDICINE devoted to endocrinology. The tumor is composed of chromaffin cells, and the catecholamines they release usually cause dramatic hypertension. But this effect can be reversed, as was demonstrated following the first resection of a pheochromocytoma, which was performed by Dr. C. H. Mayo in 1926.

Through 1978, operations for pheochromocytoma have been performed on 206 patients at the Mayo Clinic and autopsy has revealed 41 more cases not suspected clinically. The frequency among autopsies here is about 0.13%, and the incidence among the general population about one per 200,000. The tumor may occur at any age, but its peak incidence is in the fourth and fifth decades. It is extra-adrenal in about 10% of cases, multicentric in about 10%, and bilateral in 5%. Of unilateral pheochromocytomas, 60% are in the right adrenal gland. Chromaffin cells like those that make up the pheochromocytoma occur not only in the adrenal medulla but also in the paraganglia and the carotid, aortic, and jugular bodies. Thus the location of the tumor may be anywhere from the base of the brain to the epididymis, including the interatrial cardiac septum.

About 13% of cases are malignant. This diagnosis is based on the presence of tumor cells in areas where chromaffin cells do not occur, such as lymph nodes, muscle, bone, or liver, or local invasion of other tissues adjacent to the tumor. Biochemical studies and

histologic and electron microscopic examination of the tumors cannot distinguish malignancy.

Because of the dramatic reversibility of the hypertension with surgical removal of the tumor, the inadequacy of medical treatment, and the incidence of malignancy, the possibility of pheochromocytoma should be considered in every case of hypertension.

The key to the diagnosis is the symptoms and signs that nearly always result from excessive production and release of catecholamines. All or part of this release may be episodic. The effects have no relationship to the size, location, or histologic character of the tumor. The hypertension often is difficult to manage with the usual antihypertensive programs. Clinical hints include: (1) unusual lability of blood pressure; (2) symptomatic paroxysms of hypertension and tachyarrhythmia; (3) spells (five P's — head pain, palpitations, pallor, perspiration, hypertension); (4) accelerated hypertension; (5) hypermetabolism and recent loss of weight; (6) abnormal carbohydrate metabolism; (7) pressor response to induction of anesthesia or to any antihypertensive drugs; and (8) suprarenal or midline abdominal mass.

The paroxysms usually are alike and characteristically are sudden and short-lived (a minute to an hour). Hypertension occurs in 90% of cases — only during a paroxysm is half the cases but more persistently in the others, though even among the latter group the values fluctuate considerably. Some patients have postural hypotension, due to reduced intravascular volume as well as to inadequate reflex control of the arterial and venous circulation. Sufficient ischemia to cause cortical blindness, intermittent claudication, and ischemic ulcers has been seen. Hypotension has been a

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presenting feature in unusual cases of tumors that secrete mostly epinephrine, dopa, and dopamine.

Marked elevation of catecholamines can produce acute and chronic myocardial pathology and signs of transmural myocardial infarction; but the electrocardiographic changes, including Q waves, are much more evanescent than in coronary artery disease. Patients with resistant tachyarrhythmia should also be considered for the diagnosis of pheochromocytoma. Our postmortem study of 41 cases of unsuspected pheochromocytoma revealed that half of the patients had had hypertension, although the remainder were relatively asymptomatic. Death was due to pheochromocytoma in three-quarters of these cases, mostly by way of intraoperative hypertensive crises, stroke, congestive failure, or myocardial infarction. Thus, even asymptomatic and otherwise unidentifiable masses above the kidneys or in the midline of the abdomen should occasion a screening test for pheochromocytoma.

Other *associated findings* may suggest the possibility of pheochromocytoma. Cholelithiasis is seen in 23% of cases, for reasons unknown. Neurofibromatosis is seen in 2% of pheochromocytoma cases. It should be noted that patients with neurofibromatosis also may have a unique form of vascular dysplasia that may result in renovascular stenosis and hypertension as well.

Multiple endocrine neoplasia (MEN), type 2, is present in about 7% of pheochromocytoma cases with negative family history. About 19% of cases of medullary carcinoma of the thyroid with negative family history are index cases to this syndrome as well. Of autosomal-dominant inheritance, the syndrome consists of two types: (1) MEN 2a: medullary carcinoma of the thyroid, pheochromocytoma, and chief cell parathyroid hyperplasia; and (2) MEN 2b: orofacial neuromas, often associated with Marfan's habitus and medullated corneal nerve fibers, medullary carcinoma of the thyroid, and pheochromocytoma. These pheochromocytomas usually are multiple and bilateral.

Although the majority of pheochromocytomas in MEN have been in the adrenal glands, some extra-adrenal tumors have been reported as well. Adrenal medullary hyperplasia is a precursor of multicentric pheochromocytoma in this syndrome, but the existence of adrenal medullary hyperplasia in situations other than MEN is still putative. The thyroid cancer should be sought by screening determinations of calcitonin under basal conditions and after pentagastrin stimulation, and the pheochromocytoma should be

evaluated by the proportion of epinephrine in the catecholamines secreted into the blood and excreted in the urine as well as by the usual measurement of catecholamines (see below). Pheochromocytoma is a major cause of death in MEN (by cardiovascular catastrophes and malignancy).

We also have described: (1) a nonfamilial syndrome occurring predominantly in young women with extra-adrenal functioning paragangliomas, multiple gastric epithelioid leiomyosarcoma, and benign chondromas of the lung; (2) an autosomal-dominant familial syndrome of pheochromocytoma with islet cell tumors of the pancreas; and (3) the coexistence of acromegaly with pheochromocytoma. Hypercalcemia can be seen in association with ectopic production of calcitonin or parathormone by pheochromocytomas, and these tumors have also produced ACTH. Renovascular hypertension has been reported on occasion from compression of the renal artery by the pheochromocytoma.

The diagnosis is confirmed by *abnormalities in catecholamine biochemistry*. Diagnostic studies involve measuring urinary excretion of norepinephrine, epinephrine, dopamine, total metanephrines, and vanillylmandelic acid (VMA). There may be considerable daily variation in the excretion of these substances, but determination of total metanephrines has given the fewest false negatives, about 2%, and has been our choice for a screening test because of its accuracy and the ease of processing many specimens each day. Methylglucamine (a component of many iodinated contrast media used in radiology) may cause metanephrine values to be falsely normal for 72 hours after its use.

Recently methods using high-pressure liquid chromatography for the determination of fractionated catecholamines in the urine have yielded very high specificity and sensitivity as well: more than 90% of tumor patients have had positive results with only 3% false positives. The results of this test can be obscured by high doses of methyl dopa or doses of mandelamine. The determinations of VMA are positive in 90% of pheochromocytoma cases as well. These are extremely useful methods in confirming the other biochemical abnormalities, but are not yet suitable for screening large numbers of patients. The specific measurement of epinephrine can be of considerable value in diagnosis of MEN 2 or other tumors that produce epinephrine almost exclusively. These urine determinations may be carried out on specimens collected in 24 hours or shorter periods (particularly overnight), and the results may be expressed either as hourly rates



or per milligram of creatinine.

It is very important to confirm the diagnosis with several determinations of urinary catecholamines and metabolites. Recently we had a case of factitious pheochromocytoma in which the patient, a nurse, was putting epinephrine into her urine collections. The diagnosis was suspected because there was no increase of any other catecholamine or metabolite.

The application of much more specific methods (radio-enzymatic; high-pressure liquid chromatography) for measuring catecholamines in plasma also has added to our diagnostic success. Careful attention must be paid to the circumstances of blood drawing and the preparation of the patient to enhance accuracy. When accompanied by a provocative pharmacologic test such as glucagon or histamine, these newer techniques for plasma catecholamines have been very useful in excluding pheochromocytoma when urine studies have been negative but clinical suspicion continues.

If clinical and biochemical studies strongly suggest pheochromocytoma, the tumor may often be localized preoperatively by various techniques. Attempts at localization help the surgeon to plan his procedure and also help to forestall negative laparotomy if the tumor happens to be outside the abdomen. However, the surgeon still must seek multiple and bilateral tumors, since the second tumor — and further tumors — may be quite small. At present, computerized tomography (CT) seems to have emerged as the best method of preoperative localization: approximately 90% of tumors are distinguishable if included in the area examined (Figure 1).

In our practice, CT is replacing nephrotomography and angiography as the imaging method of choice because it is accurate, noninvasive, reproducible, and less hazardous than angiography. In addition, it is the only imaging technique that can depict the normal adrenal glands in equivocal cases (Figure 2).

Ultrasonography, another noninvasive method, has provided some success, especially with larger tumors, but is limited in detection of smaller lesions and tumors in the left adrenal. Radionuclide scan methods are not yet effective.

A note of caution for the clinician considering referral of a patient for a CT scan is that glucagon administered intravenously to diminish CT artifacts due to bowel peristalsis can provoke an attack in a patient with pheochromocytoma. The need for glucagon administration will decrease as CT scanners with faster scan times become more available.

Another technical suggestion is that if the adrenal

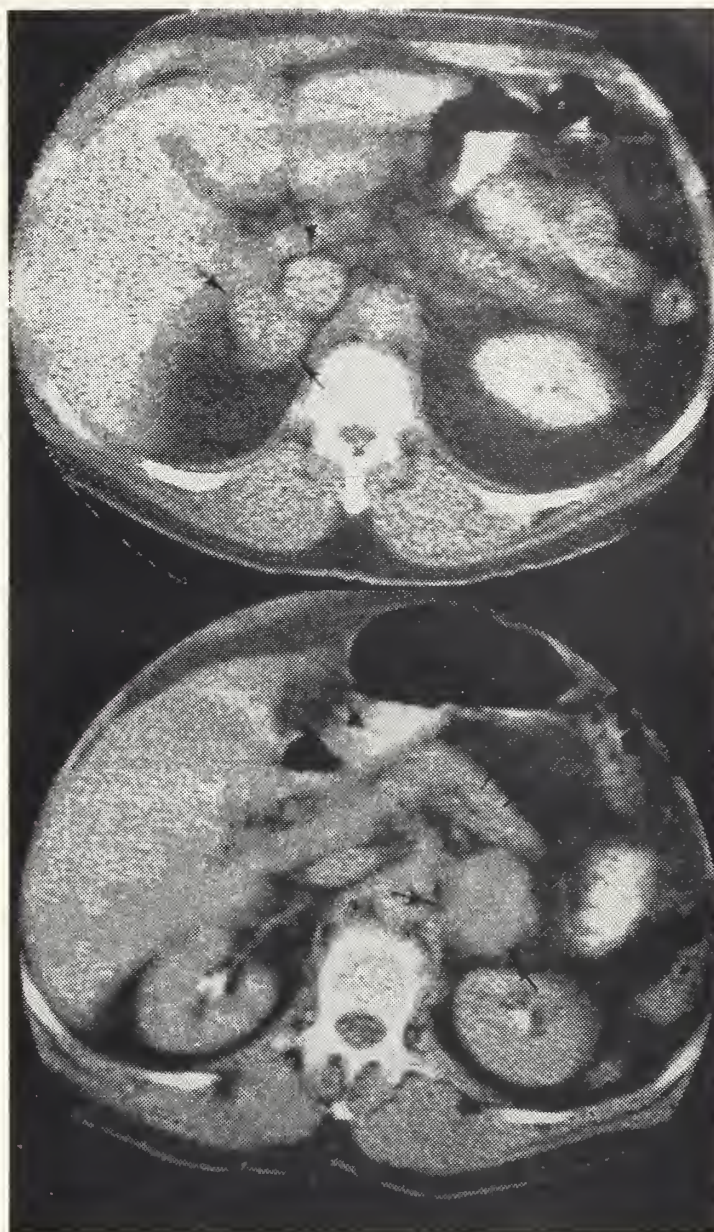


Fig. 1 — Pheochromocytomas. (A — top) 3.5-cm tumor of right adrenal gland (arrows) behind inferior vena cava (arrowhead). (B-bottom) 4.0-cm tumor of left adrenal gland (arrow) behind the body of the pancreas (arrowheads), lateral to aorta and anterior to upper pole of left kidney.



Fig. 2 — Normal right and left adrenal glands (arrows) are visible on most upper abdominal CT scans.



glands appear normal on CT scans of a patient with strong biochemical evidence of a tumor, the examination should be continued to include the remainder of the abdomen and pelvis in an effort to locate an ectopic lesion.

If imaging methods do not succeed, determinations of catecholamines on selective, sequential blood samples from the venous system may suggest the general location of the tumor.

When all else fails and clinical suspicion continues, it is important that the patient going home be provided with a 24-hour urine container (and preservative) for collection of a specimen after what he considers a typical paroxysm. Sent to the laboratory, this is tested for metanephrines, catecholamines, and VMA.

The surgical morbidity attendant upon removal of pheochromocytomas has been greatly reduced by *preparation for surgery* by appropriate alpha- and beta-adrenergic blockade (with phenoxybenzamine and propranolol, respectively) and selection of anesthetic agents that do not sensitize the myocardium to circulating catecholamines. The total operative mortality with this operation at the Mayo Clinic through 1978 was 4%. The preoperative adrenergic blockade restores the blood volume toward normal, and transfusion during the operative procedure is seldom needed. The postoperative hypotension so common in the past is now a rarity. Careful monitoring of arterial and venous pressures and the electrocardiogram, and ready availability of parenteral alpha- and beta-adrenergic blocking agents and nitroprusside during the procedure, also have contributed greatly to surgical success. Steroid preparation should be considered for those patients considered to have bilateral tumors, as in MEN 2.

High-dosage roentgen therapy can arrest tumor growth in inoperable cases, but no chemotherapeutic

agent has been demonstrated to be of value. Alpha- and beta-adrenergic blocking drugs and the rate-limiting enzyme inhibitor alphanethylparatyrosine are very valuable in controlling the symptoms of tumors. The alpha<sub>1</sub>-adrenergic inhibitor prazosin also can be used in management of pheochromocytoma. Sodium nitroprusside infusions are highly effective in controlling blood pressure as well. Labetalol, a new drug which is both beta- and alpha-adrenergic blocking (four to 16 times beta/alpha), has also been of value, but it may sometimes raise the blood pressure, depending on the relative amounts of epinephrine and norepinephrine produced by the tumor.

The *follow-up* of patients after curative surgery reveals that about 10% of cases recur, so catecholamines and metabolites should be measured annually for at least 5 years. About one quarter of those cured patients who had had persistent hypertension may continue to have hypertension. Rarely does a cured patient who had mostly paroxysmal hypertension keep on having a hypertensive problem subsequently. Among cases of malignant tumor, five-year survivorship is 44%. It is noteworthy that pulmonary metastases bring a very poor prognosis, whereas patients with involvement of other organs, including the liver, may have a very long survival.

Although pheochromocytoma is a rare cause of hypertension, the relative ease of diagnosis and treatment should persuade the clinician to give serious consideration to the possibility of this diagnosis in his assessment of all patients with hypertension, indeterminate "spells," and large abdominal masses. In the interpretation of abnormal chemistries, corroboration with other biochemical parameters should be sought; and the clinician should be concerned about preoperative localization of the tumor and appropriate preparation of the patient for surgery.

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# Hypoglycemia in the Adult

## Basic Concepts and Clinical Disorders

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Significant hypoglycemia is uncommon despite the recent popularization of the subject in the non-medical literature. The diagnosis should only be made when there is clearly an abnormally low glucose concentration, typical and reproducible signs and symptoms of a low or rapidly declining glucose concentration and prompt attenuation of these signs and symptoms by glucose administration. When significant hypoglycemia occurs and is documented chemically, a thorough search for its cause must be made since hypoglycemia is a symptom and not a disease of itself. In particular, fasting hypoglycemia nearly always indicates the presence of a serious underlying abnormality.

**I**N 1924 HARRIS proposed the concept of endogenous hyperinsulinism as a cause of hypoglycemia<sup>1</sup>. In 1927 Wilder, et al., described the first case of an insulin producing pancreatic tumor producing intractable hypoglycemia<sup>2</sup>. Since that time numerous causes of hypoglycemia have been described.

In recent years hypoglycemia as an explanation for emotional problems ranging from anxiety to schizophrenia has gained much popularity, especially in the nonmedical literature. Despite this recent popularization of hypoglycemia, significant symptomatic hypoglycemia remains relatively uncommon. Furthermore, it is important to remember that fasting hypoglycemia is not a disease in itself but a manifestation of disease.

Hypoglycemia can be defined as an abnormally (or statistically) low blood (or plasma) glucose. However, clinically this definition is inadequate for several reasons. First, the actual level below which the glucose concentration is inadequate to meet the body's requirements is not constant. Second, symptoms of hypoglycemia may appear at different glucose concentrations in different patients and in the same patient. Third, symptoms may appear at normal or even slightly elevated glucose levels in some persons when the glucose concentration is rapidly falling. Fourth, it is often difficult to determine whether a low glucose concentration is the cause of the patient's complaint.

Finally, some patients tend to over-respond to minor symptoms of hypoglycemia. Many of these individuals are tense and anxious and many have increased gastric acidity and gut motility.

The importance of an adequate blood glucose concentration lies in the fact that the brain requires glucose for 90% of its energy except during prolonged fasting. This dependence on glucose is compounded by the brain's lack of storage of significant amounts of carbohydrate. With a deficiency of glucose, the brain may suffer irreparable damage.

### Normal Values

Until recently it was not appreciated that there is a striking sex difference in fasting glucose concentrations. In 60 normal, nonobese women studied by Merimee and Tyson, plasma glucose measured by a glucose oxidase method decreased from a mean of 83 mg/dl to 63, 46 and 48 mg/dl at 24, 48 and 72 hours of fasting respectively<sup>3</sup>. Concomitant insulin concentrations were 12  $\mu$ U/ml in the basal state and 6, 3 and 4  $\mu$ U/ml at 24, 48 and 72 hours, respectively. Several of these normal women had glucose values between 25 and 30 mg/dl. In each of these subjects the ratio of immunoreactive insulin to glucose (IRI/G) decreased during fasting. In normal, nonobese males the glucose values were 85, 83, 78 and 71 mg/dl in the basal state and after 24, 48 and 72 hours of fasting, respectively. Corresponding insulin levels at these times were 14, 9, 8 and 6  $\mu$ U/ml. The IRI/G again decreased and was similar to women. Other studies have confirmed these findings. The lowest glucose concentration in women in response to fasting in four different studies were 26

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mg/dl<sup>3</sup>, 36 mg/dl<sup>4</sup>, 47 mg/dl<sup>5</sup> and 22 mg/dl<sup>6</sup>. None of these normal women had symptoms that were related specifically to the glucose level. In men the glucose concentration was never lower than 50 mg/dl during the 72 hour fast<sup>3</sup>. In obese individuals the sex difference is lost<sup>3</sup>.

Ahmed, et al.<sup>7</sup>, have studied normal young males and females ingesting meals consisting of usual American foods containing mixtures of fat, carbohydrate and protein recommended by the National Academy of Sciences and considered to be nutritionally sound. Following breakfast the plasma glucose concentration regularly decreased below the fasting value in women (mean postprandial value 63 mg/dl., mean fasting value 81 mg/dl), although none developed symptoms compatible with hypoglycemia. A similar decrease was not noted after lunch or dinner. In men the mean postprandial glucose concentration was never lower than the fasting concentration. Thus, the circulating glucose concentration normally is lower in women than in men, both with starvation and postprandially, at least in the morning. These differences must be considered when attributing symptoms to hypoglycemia. The reasons for the lower glucose levels during fasting and postprandially in women are not known. They cannot be attributed to a reduced glucagon concentration<sup>6</sup>. In pregnancy at 16-22 weeks of gestation, fasting also resulted in glucose levels 10-20 mg/dl lower than in normal nonpregnant women<sup>5</sup>. The lower glucose levels were thought to be secondary to utilization of glucose and gluconeogenic precursors by the fetus.

### Clinical Hypoglycemia

The signs and symptoms of hypoglycemia are varied but can be divided into two groups, those which arise from increased adrenergic activity and those which arise from an inadequate supply of glucose to the brain. The various signs and symptoms are shown in Table 1. In general, the adrenergic signs and symptoms are associated with a rapid fall in blood glucose and may not correlate well with the glucose concentrations obtained. With a gradual decrease in blood glucose central nervous signs and symptoms are more common but they rarely occur unless the true plasma glucose level reaches very low levels, i.e. 30 mg/dl or less. It is obvious that the signs and symptoms of hypoglycemia are non-specific and may result from a variety of other diseases.

When presented with a patient who has symptoms compatible with hypoglycemia the clinician is confronted with two problems, first to determine that

significant hypoglycemia is present, and second, to determine the cause of the hypoglycemia. In order to diagnose clinically significant hypoglycemia the following criteria should be met. First, the signs and symptoms should be compatible with hypoglycemia. Second, documentation of a low plasma glucose at the time of symptoms based on the criteria as discussed above, should be present. Third, the signs and symptoms of hypoglycemia should rapidly disappear following administration of glucose unless the hypoglycemia has been prolonged and severe. In these patients the CNS findings may persist for hours to days.

The etiology of hypoglycemia also can be difficult to diagnose. For ease of discussion and because they are mechanistically different, the causes of hypoglycemia

TABLE 1

#### Signs and Symptoms of Hypoglycemia

<u>Adrenergic-autonomic</u>	<u>Neuroglycopenic</u>
Sweating	Headache
Tremor	Visual disturbances
Tachycardia	Lethargy and lassitude
Palpitations	Irritability
Anxiety	Restlessness
Weakness	Speech disturbances
Hunger	Mental confusion, depression
Nausea and vomiting	Somnolence, stupor, coma
	Convulsions
	Hypothermia
	Bizarre neurological signs
	Personality changes
	Permanent neurological damage
	Neurologic changes of cerebrovascular disease

TABLE 2

#### Principal Causes of Hypoglycemia

##### Fasting or Spontaneous Hypoglycemia:

1. Insulinoma, beta-cell hyperplasia
2. Extrapancratic neoplasms
3. Hormone deficiency
  - a. Growth hormone deficiency
  - b. Glucocorticosteroid deficiency
4. Severe liver disease
5. Alcohol
6. Factical
7. Congenital enzyme deficiencies
8. Ketotic hypoglycemia of childhood
9. Chronic renal insufficiency
10. Drugs

##### Postprandial or Provoked Hypoglycemia:

1. Alimentary
2. Mild adult-onset diabetes mellitus
3. Reactive or functional hypoglycemia
4. Leucine sensitivity (children)
5. Enzyme deficiencies
  - a. Hereditary fructose intolerance
  - b. Galactosemia



are usually divided into those which occur during fasting and those which occur postprandially. The major etiologies for hypoglycemia are shown in Table 2. The most frequent cause of hypoglycemia, the over treatment of diabetes mellitus with insulin, will not be discussed in this review. Also, it is beyond the scope of this review to discuss in detail the biochemical mechanisms for each hypoglycemic disorder. For more detailed discussions the reader is referred to several excellent reviews of hypoglycemia in the adult<sup>4,8,9</sup> and in infancy and childhood<sup>10,11</sup>.

### **Fasting or Spontaneous Hypoglycemia**

The major symptoms are due to central nervous system dysfunction, i.e. confusion, agitation, coma and seizures. Symptoms occur most commonly in the morning before breakfast or in the late afternoon, especially with a missed meal. The range of symptoms is wide and often symptoms of excessive adrenergic activity are seen as well, i.e. sweating, tachycardia, anxiety. Hypoglycemia in these patients is the result either of an excess of insulin or an impairment of gluconeogenesis and/or glycogenolysis. Fasting hypoglycemia usually indicates the presence of a serious underlying disease.

### ***Insulinoma***

Classically these patients present with symptoms related to impairment of brain function. Symptoms frequently are intermittent and may be present for many years before the diagnosis is made. Often because of the vague nature of the complaints the patient is labeled neurotic. Usually there are no significant physical findings during non-hypoglycemic periods unless metastatic disease is present. The majority of the tumors are small, 90 percent being 2 cm or less in diameter, with many much smaller<sup>12</sup>. They are fairly evenly distributed throughout the pancreas and can be exceedingly difficult to find during operation. A few (10%) are multicentric and approximately 10% are malignant with metastases at the time of diagnosis<sup>9</sup>. Insulinomas also occur as part of the multiple endocrine neoplasia, type I syndrome (MEN-I), and these individuals have an increased incidence of multiple islet cell tumors. In the infant distant adenomas may not be present, rather there is a diffuse hyperplasia of the islets (nesidioblastosis).

The most important diagnostic feature of an insulinoma is the demonstration of an inappropriately normal or elevated immunoreactive insulin concentration in the presence of hypoglycemia. Proinsulin also is often elevated in these patients but this is

measured in most immunoassays for insulin. In the hospital, under careful observation, the patient is fasted for up to 72 hours. During the fast, glucose and insulin levels are drawn every six hours or at the development of symptoms. With development of symptoms, after obtaining glucose and insulin levels, the fast is terminated. If after 72 hours hypoglycemia has not developed, the patient is exercised vigorously for 15-20 minutes or less vigorously for two hours. Glucose and insulin levels are obtained at the end of the exercise period or with development of symptoms. In a majority of individuals with an insulinoma, hypoglycemia occurs within the first 24 hours of fasting and often within 12 hours. Rarely can a patient be fasted for 72 hours without the development of symptomatic hypoglycemia<sup>8</sup>. The usual finding in patients with an insulinoma is a falling glucose concentration with relatively stable insulin levels. In normal individuals and with other causes of fasting hypoglycemia the IRI decreases as the glucose concentration decreases, resulting in a decreased IRI/glucose ratio. In patients with an insulinoma the IRI/glucose ratio increases. The absolute IRI/glucose ratio depends on the methods of assay used for insulin and glucose and normal ranges must be determined for the laboratory used. Several stimulatory tests also have been described, i.e., Tolbutamide, glucagon and leucine tolerance tests. However, these tests are rarely indicated. Insulin suppression tests have also been described. In one, fish insulin, which is biologically active but not measured in the radioimmunoassay for human insulin, is administered and the IRI is observed for failure to suppress. In another, regular insulin is given and the suppressibility of C-peptide is observed. These also have only limited utility.

The treatment for insulinoma is surgical. When surgical treatment is not possible or while awaiting surgery, symptomatic medical treatment may be required. This consists of frequent feedings of a high carbohydrate diet and a trial of glucocorticosteroid treatment. Long acting glucagon preparations have been tried experimentally as well. In addition diazoxide, which suppresses insulin secretion, may be tried. Streptozotocin currently is the treatment of choice for symptomatic metastatic islet cell tumors. It is used alone or in combination with other anti-neoplastic agents<sup>9</sup>.

### ***Extra-pancreatic Neoplasms***

These tumors are almost always large and are usually obvious on physical examination. They are predominantly of mesenchymal or hepatic origin. The etiology of hypoglycemia is not well understood but



may be related to increased glucose utilization by the tumor or impaired glucose production by the liver. Increased peripheral glucose utilization from elevated levels of nonsuppressible insulin-like activity (NSILA) elaborated by the tumor or defective counterregulatory mechanisms such as impaired glucagon responsiveness have also been suggested as mechanisms. Occasionally these tumors may cause hyperinsulinemia. This has been reported with a carcinoid tumor and we have seen one patient with an elevated IRI who had a hepatoma. Treatment is removal of the tumor where possible. Even partial removal of the tumor may be of benefit.

#### *Hormonal Deficiency*

Fasting hypoglycemia may result from both glucocorticosteroid and growth hormone deficiencies. Patients with glucocorticoid deficiency are very sensitive to hypoglycemic agents. The reduced glucose concentration in subjects with glucocorticoid deficiency is due to a reduced rate of gluconeogenesis by the liver. The mechanism of hypoglycemia in growth hormone deficiency is not well understood. These individuals have an increased sensitivity to insulin but the mechanism by which growth hormone influences insulin sensitivity is not known. Treatment of the underlying hormonal deficiency corrects the hypoglycemia.

#### *Liver Diseases*

In severe hepatocellular diseases or with extensive malignant replacement of the liver, hypoglycemia may become manifest. Most likely the hypoglycemia is a result of insufficient hepatic tissue for adequate glycogen storage, glycogenolysis and gluconeogenesis.

#### *Alcohol-induced Hypoglycemia*

Alcohol ingestion during fasting may result in prolonged and severe hypoglycemia, especially in chronic alcoholics, in binge drinkers, and in children. Several mechanisms have been proposed. The major defect appears to be a decrease in the NAD/NADH ratio as a consequence of rapid metabolism of ethanol. This inhibits gluconeogenesis. Unfortunately, alcohol-induced hypoglycemia frequently goes unrecognized, the symptoms being attributed solely to intoxication. As a consequence, the mortality is substantial.<sup>13</sup>

#### *Facticial Hypoglycemia*

Facticial, or self-induced hypoglycemia should be suspected when there are sporadic symptoms not

related to meals, exercise or other factors. The syndrome is most often seen in medical and paramedical personnel or in relatives of diabetics, many of whom have a history of psychiatric illness. When hypoglycemia is the result of secretive insulin administration, the diagnosis can be made by the demonstration of low levels of C-peptide associated with high IRI levels during an episode of hypoglycemia. Additionally, insulin antibodies may be found in the non-diabetic patient. When ingestion of oral hypoglycemic agents is suspected as an etiology of hypoglycemia, blood or urine samples should be obtained for drug or drug metabolite determinations.

#### **Postprandial or Provoked Hypoglycemia**

In general the symptoms of postprandial hypoglycemia are mild and are secondary to excessive adrenergic activity. In addition, the tolerance to these symptoms appears to vary greatly among individual patients. Those who are anxious and emotionally labile and who frequently have a variety of other complaints are more frequently seen by the clinician. Historically these patients relate the onset of symptoms between two to five hours after a meal, especially a high carbohydrate meal. The most common diagnostic procedure is the five hour oral glucose tolerance test (OGTT). This is done to determine if hypoglycemia occurs and if that patient's usual signs and symptoms are reproduced.

#### *Alimentary Hypoglycemia*

This term refers to postprandial hypoglycemia in patients who have had previous gastrointestinal surgery, usually partial gastrectomy or vagotomy and pyloroplasty, and occasionally in patients with other gastrointestinal abnormalities such as peptic ulcer disease. In these individuals, carbohydrate is rapidly absorbed. This is followed by a proportionate rapid and excessive insulin rise. The net result is a rapid glucose fall off reaching a nadir 1.5-3 hours after the meal. Although many patients have glucose levels below 50 mg/dl, a much smaller number have significant symptoms. The treatment consists of a low carbohydrate diet given in frequent small feedings. Additionally, anticholinergic agents to decrease gastrointestinal motility may be useful. Recently propranolol, 10 mg before meals, has been used.<sup>9,14</sup> Propranolol appears to moderate the decrease in glucose as well as inhibit the adrenergic symptoms.

#### *Mild Adult Onset Diabetes Mellitus*

Some patients with early adult onset diabetes mellitus develop symptoms of hypoglycemia three to



five hours after a glucose load or carbohydrate meal. The five hour OGTT typically shows an early hyperglycemia with a delayed insulin response, then hypoglycemia in the late postprandial period. The basis of these findings is not fully explained. Nonetheless, the treatment is weight reduction when necessary and a low carbohydrate diet.

#### *Reactive or Functional Hypoglycemia*

The question must first be raised as to whether this diagnosis exists as a pathologic entity. It is in this group in the last 10-15 years that a large number of patients have presented with the self-diagnosis (sometimes medically "confirmed") of hypoglycemia based on a wide variety of non-specific complaints ranging from chronic fatigue, lethargy, nervousness, to the 5 p.m. 'dwindles'.<sup>15</sup> These symptoms are supposedly relieved by food or alcohol intake. Again it must be noted that many of these individuals are anxious, tense persons. It is also important to recognize that the changes in glucose and insulin and in other substrates

are normal and appropriate in the vast majority of these individuals. In the words of Merimee, "This is a classic example of the axiom that false standards create false disease".<sup>8</sup> Park, et al.,<sup>16</sup> have demonstrated that nearly one-fourth of normal subjects have nadir glucose concentrations under 50 mg/dl at some time during the OGTT. On occasion values as low as 35 mg/dl were seen without the development of symptoms. Thus it is our belief that this 'entity' has been and continues to be greatly overdiagnosed. However, a small number of patients do develop distressing, classical signs and symptoms of adrenergic stimulation associated with a decrease in plasma glucose. In these patients there is a delayed and inappropriately prolonged insulin response to a carbohydrate challenge.<sup>17</sup> Subsequent hypoglycemia occurs. Treatment of these patients consists of a low CHO diet as described above and small doses of propranolol if dietary management is unsuccessful. Anticholinergics may also be tried.

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#### *Parathyroid Disorders — Hanley and Brown (page 483).*



# Management of Adult Diabetes Mellitus

WAYNE F. LEEBAW, M.D.\* and RAYMOND L. MARECEK, M.D.\*

A review of the basic principles in the management of the adult with diabetes mellitus is presented. A protocol for following the individual patient is outlined and therapy with oral agents and insulin is discussed. Parameters of measuring control and treatment of special problems are also considered.

**T**HE PAST TWENTY YEARS have witnessed major changes in our viewpoints as to the significance, pathogenesis and treatment of maturity onset diabetes mellitus. We are now aware this disease is more serious than once thought. There is a high probability for coronary artery disease, peripheral vascular disease, neuropathy, cataracts, retinopathy and renal disease — complications once thought to be outcomes only of juvenile-onset (insulin-dependent) diabetes mellitus.

We are now aware of the major role of obesity in the development of maturity onset diabetes. Obesity or overeating seems to result in a resistance to insulin action,<sup>1</sup> i.e., more insulin than normal is needed to perform the same metabolic effect. As one becomes more obese, more insulin must be secreted to maintain a normal blood glucose. The concept of hormone receptors may explain why one can have high blood glucose in spite of large amounts of native insulin (insulin resistance). The ability to lower blood glucose is dependent not only upon the amount of circulating insulin but the concentration and affinity of insulin receptors on the outer plasma membrane of the target tissue (liver, muscle, fat). There are many steps beyond the binding of insulin to the receptor which may influence insulin action as well.

Obesity alone may not be entirely responsible for the insulin resistance in this disease as Reaven & Olefsky<sup>2</sup> present good clinical evidence that many "chemical" diabetics (normal FBS but abnormal glucose tolerance test) are lean but have resistance to insulin.

Though the pathogenesis of maturity onset diabetes is unclear, it seems unlikely it is due simply to a relative deficiency of insulin. Therefore, the therapeutic approach is far more complicated than that for primary hypothyroidism where replacement of thyroid

hormone alone clearly alleviates the symptoms and prevents the complications of hypothyroidism.

The therapy for maturity onset diabetes includes short term and long term goals (Table 1). There is general agreement concerning achievement of the first five short term goals, but some disagreement as to whether the sixth goal will effect any change on the long term goal. There is an increasing body of evidence in experimental animals that hyperglycemia alone does contribute to some of the vascular complications of diabetes and euglycemia presumably would forestall or prevent their development.<sup>3,4,5</sup>

The controversy regarding diabetes management has been heightened by the report of the University Group Diabetes Program (UGDP) initially published in 1970.<sup>6</sup> The original conclusions indicated the sulfonylureas had no role to play in this disease and in fact could even contribute to cardiovascular mortality. Recent additional conclusions from the UGDP<sup>7</sup> indicate even insulin may be no better than placebo in reducing mortality and non-fatal vascular complications in diabetics. However, a recent policy statement in January 1979 by the ADA<sup>8</sup> presents the following viewpoint among others . . . "significant differences do exist between the therapeutic designs of the UGDP protocol initiated in 1961 and the medical strategies

TABLE 1

## Short Term Goals of Therapy

1. Absence of diabetic ketoacidosis/coma.
2. Absence of severe hypoglycemic reactions
3. General sense of well-being (freedom from symptoms of diabetes)
4. Normal weight
5. Absence of significant glycosuria
6. Blood glucoses in normal or near normal range for age (FBS: 125, 3 hour p.c.: 150-175)

## Long Term Goals of Therapy

Prevention or delay in appearance of diabetic complications

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commonly applied in 1979 by physicians with respect to the management of maturity-onset diabetes . . ."

The ADA in their statement also makes the following recommendations among others . . .

. . . "until a review of all newer data which relate to the UGDP findings has been completed, any formal recommendations on the use of tolbutamide in maturity onset diabetes that are based on the initial findings of the UGDP study should be held in abeyance . . ."

One should not at this time exclude any mode of therapy whether it be diet, sulfonylurea or insulin<sup>9</sup> in order to achieve the goals outlined. We subscribe to all of the short-term goals and likewise feel the long term goal can be effected by control of blood glucose and the following treatment protocol is based on that premise.

### **An Approach to the Individual with Diabetes**

#### *Evaluation of the Patient*

1. Age
2. Height and weight
3. Past history and complicating medical problems
4. Physical exam
5. Dietary habits and alcohol consumption
6. Amount of physical activity (work-related and leisure-related)
7. Basic lab data including CBC, urinalysis, 3-hour post prandial blood glucose, EKG, FBS, fasting triglyceride, cholesterol, BUN, creatinine, electrolytes.

#### *Identify Short-Term Goals for Each Patient*

Diet to achieve ideal body weight is based on present weight and physical activity and desire to lose one and a half to two pounds per week.<sup>10</sup> The diet must also include the unique food preferences of the patient (should be done by a dietician if possible). We strongly recommend the principles of dietary therapy recently outlined by the American Diabetes Association.<sup>11</sup> (Reprints available from the ADA for \$.50)

Determine relative risk of hypoglycemic agent (sulfonylurea or insulin).

a. If greater than 70 years of age, there is a significant risk of harm associated with hypoglycemia. One should not attempt rigid blood glucose control.

b. In the presence of significant complicating medical problems such as underlying heart disease, endocrine disease (hypopituitarism, hypoadrenalism), renal disease or liver disease (and/or moderate alcohol consumption) one should be *extremely* cautious about rigid blood glucose control.

c. Absolute contraindications to sulfonylureas are patients who are: pregnant, ketosis-prone, or undergoing surgery as well as those who have significant

infections, renal disease or liver disease.

#### *Implement Plan to Achieve Short Term Goals*

Routine visits should be both informative and timely.

1. Informative visits should assess
  - a. Weight and blood pressure
  - b. Degree of compliance with diet and urine testing.
  - c. Pattern of urine test results with double-voided urines.
  - d. Pattern of hypoglycemic reactions (number, frequency, and timing in relation to meals and hypoglycemic agent.)
  - e. Various aspects of physical exam as indicated. Emphasize:
    - (1) Annual fundoscopic exam in office and referral to ophthalmologist if any proliferative retinopathy.
    - (2) Review of foot care and foot exam.
  - f. Periodic blood glucoses to determine renal threshold for glucose and ensure control is as satisfactory as urine tests may indicate.
2. Timely visits

Follow up of initial visit should be within one to two weeks to demonstrate interest in patient achievement of goals and to encourage questions and communication. This also often obviates the need for hospitalization during this early phase of management.

Frequency of visits thereafter may vary from 4 to 12 weeks or longer. If there is failure to achieve most short term goals then obviously a change in approach is necessary which may include either initiation of sulfonylurea or insulin (see below) or an increase in dosage of the respective agent. When changes in medication are made visits every four weeks are most advisable.

#### *Assess Outcome of Therapeutic Approach. (Table 2)*

A periodic review of all short-term goals should be made every 3-6 months. Measures which may help determine whether satisfactory control of blood

**TABLE 2**

#### **Parameters of Measuring Control**

1. Diabetic urines a.c. and h.s. — double-voided
2. Blood glucose monitoring
  - In office
  - Home (dextrostix)
3. 24 hour urine glucose
  - Fractionated if necessary
4. Hbg. A1C
5. Triglyceride levels



glucose has been achieved are:

1. Diabetic urines — We consider it extremely important that our patients follow their double-voided urines pre-meal at least three times a day and if control is rather labile, four times a day. (The urines only need to be double-voided if there is glycosuria.) Each time we see the diabetic in the office, we review this written record. We also ask our diabetics to make a record of the time and frequency of reactions and to write down an explanation as to why they think they might have had a reaction. The diabetic urines are probably the most valuable tool in providing day-to-day monitoring of control and also in assisting us and our patients in deciding whether or not to add regular insulin or to go to a second injection of insulin in the late afternoon. (See section on insulin therapy.)
2. Blood glucoses
3. Twenty-four hour urine glucose — If less than 20 grams of glucose spilled per 24 hours, control is considered good. (Very good if less than 5% of total CHO intake.)
4. The Hemoglobin A1C ("Fast Hemoglobin"; Glycosolated Hemoglobin): This is a relatively new test that is still undergoing extensive clinical investigation.<sup>12,13</sup> It is a relatively inexpensive test that has the advantage of measuring or quantitating "tertiary" control of diabetes. Glucose is irreversibly attached to hemoglobin A, forming hemoglobin A1C during the 120-day life span of a red blood cell. This transglycosylation reaction occurs in everybody and depending on the lab in which the hemoglobin A1C is measured, normal levels of between 6 and 9 percent of hemoglobin A1C are present. If there is a significant elevation in the mean blood sugar over a long period of time, this will result in an elevation or increase in the percent of hemoglobin A1C. Diabetics, therefore, have a percent of hemoglobin A1C that's usually greater than 10

percent. Certain laboratories will indicate degrees of abnormality based on clinical studies of large populations of diabetics. We find ourselves using the glycosolated hemoglobin more and more frequently. It is especially valuable in those patients who have labile diabetic urines and who are generally nonketotic. In these patients a normal or relatively low hemoglobin A1C reassures us that their control is probably adequate.

### Drug Therapy in Diabetes

#### Sulfonylureas

##### 1. Types and Adverse Effects.

The varieties of sulfonylurea agents currently available are outlined in Table 3. As will be noted the major differences relate to duration of action and dose range. One should become familiar with one type of sulfonylurea and its side effect. If blood glucose control is unsatisfactory when the agent is pushed to the maximum effective dosage, it is unlikely other sulfonylureas will succeed.

The most common and disturbing side effect we have found with the usage of these agents is the disulfiram-like reaction to alcohol. This manifests itself as a transient flushing episode with sweating, headaches, nausea, and cramps. The patient should be reassured this is simply a side effect of the drug and should avoid alcoholic beverages.

Occasionally hyponatremia will be noted due to the antidiuretic effects of these agents but rarely does this necessitate discontinuation.

The principal limitation to chlorpropamide is the prolonged half-life. Should hypoglycemia develop one must recognize that repeated episodes of hypoglycemia may recur and observe the patient in the hospital until hypoglycemia resolves.

##### 2. Mode of Action

Although the mechanism of antidiabetic

**TABLE 3**  
**Sulfonylurea Agents**

Type	Available Form	Total Daily Dose (mg)	Duration of Action (hr)	Times Given
Tolbutamide (Orinase)	500 mg	500-2000 mg	6-12	BID-TID
Chlorpropamide (Diabinese)	100 and 250 mg	100 and 250 mg	Up to 60	Once daily to BID
Acetohexamide (Dymelor)	250 and 500 mg	250-1500 mg	12-24	Once daily to TID
Tolazamide (Tolinase)	100 and 250 mg	100-1000 mg	12-24	Once daily to BID



action of the sulfonylureas is not fully established, it is quite clear chronic therapy does not simply stimulate pancreatic insulin secretion<sup>14</sup> as noted during experiments with acute administration of the drug. Evidence now indicates the sulfonylureas administered chronically enhance insulin action at the target tissue level (liver,<sup>15</sup> muscle<sup>16</sup>). This enhanced insulin effect may be mediated through increased numbers of insulin receptors. However, precise identification of the site of action must await further studies.

### 3. When to Use

It is often useful to add a sulfonylurea to facilitate management in carefully selected patients (see approach to the individual, item B, Relative Risk of Hypoglycemic Agent) to control hyperglycemia. The agent will generally reduce the symptoms of hyperglycemia and improve the sense of well being promptly while attempts are made to achieve ideal body weight. One would like to achieve all of the short term goals as quickly as possible and the sulfonylureas do at times make a significant contribution to treatment. One must add a warning — often initiating simultaneously diet and sulfonylurea agent together may result in hypoglycemia. If the patient is stable and not very symptomatic, diet and weight loss should have first priority.

It is of utmost importance to emphasize the ultimate objectives of normal blood glucose (FBS less than 125 mg/dl and three hour postprandial less than 150-175 mg/dl and normal body weight on *diet alone*. With this in mind attempts should be made periodically to reduce or discontinue the sulfonylureas whenever the short term goals are achieved.

### Insulin Therapy

#### 1. Types of Insulin

The insulin that is commercially available in this country is most often a mixture of beef and pork insulin (95%) with the remainder mono-species pork and mono-species beef insulin. There has been a gradual increase in the purity of insulin and since 1972 all

commercial insulin now contains 99% insulin and insulin-like materials and less than 1% of other materials of higher molecular weight. This so-called "single-peak insulin" has been even further purified by DEAE cellulose chromatography resulting in single-component insulin that is 99% pure insulin.<sup>17,18</sup> Insulin is presently sold in four concentrations: U-40, U-80, U-100 and U-500, but the U-40 and U-80 insulins are being phased out and will soon no longer be available.

There are three basic types of insulin used in clinical practice — short acting; intermediate acting; and prolonged or long acting. Each of these three types vary with respect to peak concentration as well as time of peak activity and duration of activity. The types of insulin are summarized in Table 4. The most commonly used insulins are regular and NPH or Lente. There is not a great need for use of the long-acting insulins at the present time. Lente and NPH insulins for all practical purposes are clinically similar and there is no distinct advantage of one over the other.

#### 2. When to Use Insulin

The two obvious non-controversial indications for insulin are in patients in diabetic ketoacidosis and those patients who would develop diabetic ketoacidosis without insulin therapy. We will also use insulin in diabetics who become hyperglycemic due to acute stress or during pregnancy (Table 5). The use of insulin may be temporary in these patients. We tend to use insulin in those adult patients who have hyperglycemia not responsive to diet or weight reduction. On certain occasions or if the patient prefers, we may turn to an

**TABLE 5**  
**Indications for Insulin Therapy**

1. **Absolute**  
Diabetic ketoacidosis  
Hyperglycemia associated with pregnancy/severe infection
2. **Suggested**  
Hyperglycemia if unresponsive to weight loss/diet/sulfonylurea agents  
Hyperglycemia associated with surgery/trauma/hyperalimentation  
Hyperosmolar coma

**TABLE 4**

Type of Insulin	Appearance	Insulin Preparations			
		Action	Onset (hour)	Peak (hour)	Duration (hour)
Regular (crystalline)	clear	Rapid	¼-1	2-4	6-8
Semi Lente	turbid	Rapid	½-2	2-4	12-16
NPH	turbid	intermediate	2-3	6-12	18-24
Lente	turbid	intermediate	1-3	6-12	18-28
Protamine Zinc (PZT)	turbid	prolonged	4-8	14-24	24-36+
Ultra Lente	turbid	prolonged	5-6	22-26	30-36



oral hypoglycemic agent in this group. (See above) Naturally the cornerstone of therapy as with all diabetics is diet, as mentioned above, but if hyperglycemia persists we will discuss the various options with the patient.

### 3. The Choice of Insulin

We always use U-100 insulin. Any new patient who comes to see us who is using U-40 or U-80 insulin is instructed on converting to U-100 insulin. We also always use an intermediate-acting insulin. Regular insulin is used in most of our patients although not all. However, all of our patients are instructed on use of regular insulin even if it's not a part of their daily regimen, so they would know how to use this form of insulin in case of an acute illness or the development of intermittent ketosis. They are also all instructed on how to mix intermediate-acting and regular insulin.

### 4. Dose and Frequency of Insulin Therapy

There is no single guideline on insulin therapy. Individualization is required and decisions are often arbitrary. We would like to emphasize the following major points:

- a. Intermediate-acting and rapid-acting or regular insulin can be mixed in the same syringe. Mixing of these insulins will minimally effect the duration of action unless the ratio is very close to 1:1.
- b. Use as little insulin as necessary to achieve pre-meal normoglycemia. Obviously hypoglycemia should be avoided — as should wide swings in blood sugar that are caused by overinsulinization.
- c. The duration of actions of various insulins is simply an average and may vary considerably for no apparent reason from diabetic to diabetic.

In those patients who exhibit fasting glycosuria but who have negative urines in the afternoon or evidence of hypoglycemia in the late afternoon, we generally advise that they reduce their morning intermediate insulin and add a pre-dinner dose of intermediate insulin. These patients may be getting a "rapid" effect of their intermediate-acting insulin but the effect wears off and does not maintain euglycemia through the evening and night. They therefore need a second dose of insulin. A second group of patients may present with glycosuria throughout the day but with a negative or low urine glucose at bedtime and with occasional nocturnal reactions. They will often have negative urines in the morning or may again have significant glycosuria in the morning in response to nocturnal

hypoglycemia. (Post-hypoglycemic hyperglycemia.) The way we usually handle a patient with this pattern is to decrease the morning intermediate-acting insulin and to add or increase short-acting insulin in the morning. By adding or increasing their regular insulin, this decreases their mean glucose level through the day and by reducing their intermediate-acting insulin in the morning, this prevents the nocturnal hypoglycemia. It is thought that these patients are having a "delayed" and prolonged effect from intermediate-acting insulin.

It is important to emphasize that there will be gradations between these two so-called "classic" extremes and that the only way to ascertain where your patient fits is by close follow of the diabetic urines.<sup>18,19</sup>

### 5. The Use of Insulin in Special Circumstances

#### a. Ketoacidosis

A discussion of the pathogenesis and management of diabetic ketoacidosis is beyond the scope of this article. However, we would like to emphasize that recent evidence is overwhelming that the prior concept of insulin resistance in ketoacidosis was wrong. A low-dose regimen of insulin therapy in which doses of insulin between 5-10 units per hour are given has proved to be adequate in the treatment of diabetic ketoacidosis. According to prospective studies by Kitabchi<sup>20</sup> and others, low-dose insulin may be given subcutaneously or intramuscularly each hour or by constant intravenous infusion with similar successful results. We prefer to use a constant insulin infusion. We generally give a loading dose of 15 units of regular insulin by IV push and then follow this with a constant infusion initially at 10 units an hour. We of course closely follow the important parameters such as hourly glucoses and bicarbonate levels to be certain that our treatment is adequate. Important points to remember are that *enough* insulin has to be used and that fluid therapy is the other major cornerstone of treatment of diabetic ketoacidosis. If we do not see a decline in the initial blood sugar by at least 10 to 15 percent in the first hour, then we will give another loading dose of insulin 15 units intravenously. Our patients often require three to five liters of fluids in the first eight hours of treatment. It also goes without saying that it is very important to follow the electrolytes and to replace potassium.

We have found that this method of insulin delivery dramatically simplifies the treatment of diabetic ketoacidosis. To date we have not seen anybody fail when the parameters of blood sugar and bicarbonate are closely followed and we



have only on rare occasions had to give an additional loading dose of insulin or to increase the infusion above 10 units per hour. Because we have given no subcutaneous insulin that will be absorbed after blood sugars are in normal range, we have seen no hypoglycemia. As glucose levels fall, the insulin infusion rate is decreased appropriately.

#### b. Surgery

In our insulin dependent diabetics undergoing surgery, we generally give them half their usual dose of intermediate-acting insulin and then follow their blood sugars closely on the day of surgery. We cover them the remainder of the day with regular insulin after obtaining glucoses in the recovery room and perhaps every six hours after that if necessary.<sup>21</sup> In some circumstances the low dose insulin infusion has been used very successfully in diabetics undergoing major surgery such as kidney transplantation.

#### c. Pregnancy

Hyperglycemia and ketosis are to be strictly avoided during pregnancy since both factors contribute to serious adverse effects on the fetus.<sup>22</sup> Strenuous efforts must be made to achieve blood sugar levels that occur in the pregnant non-diabetic — a daily mean blood sugar  $\left( \frac{\text{FBS} \div 2^\circ \text{ ppbs}}{2} \right)$  between 90-100 mg percent.<sup>23</sup> In the gestational diabetic, if diet alone fails to achieve "normoglycemia" then insulin must be instituted.

Insulin requirements increase in the second and third trimester and dramatically fall in the immediate post-partum period. We follow our pregnant diabetics with FBS and 2° ppbs weekly in the last trimester.

At the time of delivery we give 1/3-1/2 of the *pre-pregnancy* insulin dose. Mintz et al have recently reviewed their experience with low-dose insulin infusion at time of delivery and more and wider experience is necessary with this technique.<sup>24</sup>

### 6. Special Problems.

#### a. Symogyi Effect of Post-Hypoglycemic Hyper-

glycemia

Most diabetologists believe that there is a period of relative insulin resistance that follows hypoglycemia. Where we see this most often is in patients who are over-insulinized and whose insulin reactions are not apparent either to the patient or to the physician. In the original description of the Symogyi Effect,<sup>25,26</sup> the patients were continuously hyperglycemic and glycosuric and suffering from chronic fatigue and lethargy. They were generally on very high doses of insulin and raising the dose of insulin proved not to have any effect. Over many months to years, this insulin dose was gradually reduced with an improvement in diabetic control as well as clinical improvement. The patients, as originally described may, in fact, be the extremely unusual. Most often the presentation of hyperinsulinism is manifested by wide fluctuations in plasma glucose and sharp fluctuations in urine glucose. Patients may show evidence of negative urine sugars and ketones in the morning and then be spilling 2% with ketonuria by noon or before dinner. The so-called "brittleness" may in fact be due to the development of subclinical hypoglycemia due to excessive insulin or poor distribution of insulin therapy. One of the diagnostic hallmarks of this problem is that increasing the dose of insulin tends to worsen rather than improve control. The treatment is, therefore, not an increase but a gradual reduction in the dose of insulin.<sup>27</sup>

### The Future

Advances in our understanding of the pathogenesis, genetics and epidemiology of diabetes are occurring at a rapid rate. This is also true regarding our ability to manage diabetes and its complications. New and improved techniques are being developed to better control blood sugar and hopefully prevent serious complications of the disease. These range from dietary changes (increase fiber) to exercise and to better delivery systems for insulin (constant subcutaneous infusion with a pump-controlled device). Hopefully further success in these areas will facilitate achievement of both the short and long-term goals in treating diabetes.

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- 9.-15. Will be found on page 466.



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# Quinamm<sup>TM</sup>

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## Brief Summary

**INDICATIONS:** For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

**CONTRAINDICATIONS:** Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

**PRECAUTIONS:** Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication. Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

**ADVERSE REACTIONS:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

## DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977  
U.S. Patent 2,985,558

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# Juvenile Onset Diabetes Mellitus

## Practical Care

DONNELL D. ETZWILER, M.D.\* and MICHAEL B. AINSLIE, M.D.†

**Diabetes mellitus affects one in every 529 school children in Minnesota. Life expectancy of these children is markedly decreased and acute, intermediate and long-term complications are a constant threat. Informed patients cooperating with knowledgeable and concerned health care professionals can make a difference. This paper describes the practical aspects of the medical management of over 500 children with diabetes in our practice.**

**D**IABETES MELLITUS is a chronic disease which affects almost 100,000 children throughout the U.S. At the present time there is no cure for diabetes and we must be content with attempting to control the disease. Children with diabetes are susceptible to acute, intermediate and long-term complications. Sudden onset of hypoglycemia and diabetic acidosis constantly threaten these children and poor control over periods of weeks or months may lead to failure of growth and development. It is the long-term complications associated with this disease, however, that are so devastating. Diabetes is now recognized as the leading cause of new blindness in those over the age of 20 and the same microvascular complications occurring in the kidney account for over 50% of the deaths of these victims. According to the National Commission on Diabetes, the mean life expectancy of a child who develops diabetes is approximately 25 years after onset of the disease.<sup>1</sup>

There is increasing evidence that proper management of these children can minimize long-term small blood vessel disease. In 1976 the American Diabetes Association published a policy statement on control stating . . . "The goals of appropriate therapy should thus include a serious effort to achieve levels of blood glucose as close to those in the non-diabetic as feasible . . . This concept is particularly applicable to the diabetics at greatest risk of developing the microvascular complications — the young and middle-

aged. . . ."<sup>2</sup>

Achieving a reasonable degree of control in most insulin-dependent juvenile diabetics is exceedingly difficult and particularly among the teenage grouping. A significant amount of physician time and skill is demanded as well as a multiplicity of health care specialists who are willing to work together with cooperative and informed patients. It is the goal of this paper to describe some of the needs, resources, goals and plans which assist in providing such comprehensive care.

### Immediate Care

The onset of diabetes in juveniles is usually rapid and sometimes fulminating. Any young individual suspected of having diabetes should have the diagnosis ruled out that day. A single blood glucose determination is usually sufficient in most children. A random sugar of 140 mg.% or above would be highly suspect and over 200 mg.% would be diagnostic. Rarely are glucose tolerance tests necessary. There is almost always a history of polyuria, polydipsia and polyphagia of recent onset. Rarely are these symptoms of over 4-6 weeks' duration and we have seen one patient who went into collapse within 48 hours after urinary frequency was first noticed. Physicians dealing with adult diabetes may not be familiar with the possible rapid course of diabetes in childhood and should be aware of its existence and sensitive to its dangers.

It is our present policy to hospitalize all newly-diagnosed children with diabetes in order to assess the severity of their disease, initiate insulin therapy and begin meal planning in a setting which provides an

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immediate educational experience.

Upon hospitalization it is important that the initial orders inform the dietary, nursing, and educational staff of the approximate duration of the patient's stay. This enables them to schedule and provide appropriate teaching programs for the family and the patient. If the child is not in diabetic acidosis, we initiate insulin therapy with low doses of subcutaneous regular insulin until the following morning. A small dose of 5 to 10 units of regular insulin is first administered in order to assess the child's sensitivity of the drug. Measuring blood sugars at two-hour intervals permits one to monitor individual responses to insulin therapy and determine the immediate requirements. The morning following the child's admission, a small dose of intermediate acting (either NPH or Lente) insulin is started. There does not appear to be any significant difference in effectiveness of either Lente or NPH insulin. Most children will require mixtures of regular and an intermediate acting insulin. After starting with low dose intermediate acting insulin, we obtain blood sugar determinations five times each day (6:30 a.m., 11:30 a.m., 4:30 p.m., 9:30 p.m. and 2:30 a.m.) and regular insulin is added as indicated. Each subsequent morning review of the previous day's experience provides a greater insight into the child's daily insulin needs.

In the early stages of insulin therapy, once an adequate dosage is attained, the insulin requirement almost immediately begins to decrease and then over a period of several weeks it plateaus. During the initial five to six days of hospitalization, an approximation of the individual's insulin needs is obtained. Upon discharge, control is monitored in the home by using urine sugar determinations and urine quantitative glucose results. In some patients blood glucose levels may be obtained using some of the new home monitoring instrumentations such as the Eytone Reflectance Meter (Ames), the Dextrometer (Ames) and the Stat-Tek (Bio-Dynamics) which permits patients to conduct these tests at home using finger-stick specimens.<sup>3-6</sup> In general, however, children are not eager to stick themselves several times each day but further investigation of this adjunct is necessary.

Although most of our newly-diagnosed patients do require a mixture of regular and intermediate insulins, we do not routinely "split" the dosage; that is, give two shots each day, one in the a.m. and one at supper time. Such "splits" are made when blood sugars and quantitative urine determinations for glucose suggest such a move is indicated. Such indications are high

bedtime and breakfast urine sugar tests and significant spills of evening and overnight sugar as measured by quantitative urines.

All patients are placed on a meal plan with roughly 1,000 basal calories plus 100 calories for each year of life up until approximately 10 years of age. Thus, the average 8 year old might require 1,000 basal calories plus 800 or a total daily caloric intake of 1,800. Variations in body size and activity patterns must also be taken into account and appropriate adjustments made. The food distribution is divided into approximately 50% carbohydrate, 30% fat and 20% protein. Three basic meals are planned along with afternoon and bedtime snacks. Mid-morning snacks are frequently included for younger patients. Additional calories must also be added to the basic plan if there has been a large weight loss during the onset of the disease and then re-evaluated three to four weeks later. Patients' food likes and dislikes must also be identified and family living patterns, needs and resources assessed. The most successful patient meal plans are best developed by knowledgeable dietitians who have the skills and time required for such comprehensive assessment.

Education is an integral part of the management of every patient with diabetes and it is important that this process be planned and formalized. Our experience has taught us to divide the educational plan into three stages with separate goals and objectives.<sup>7</sup> The *initial* patient and family educational effort begins in the physician's office when the diagnosis is made and should continue in the hospital. It is the goal of the initial educational program to inform the patient and members of the family of the diagnosis of diabetes and to provide information necessary for the immediate management of the disease. An in-depth educational experience during this period is *not* appropriate since many times these patients are acutely ill and the family is gravely concerned and worried. We limit this initial education phase to include the following topics: (1) some general information about diabetes, (2) urine testing, (3) insulin administration, (4) meal planning and (5) acute complications. The families are also informed that they will receive more education later and plans are made at the time of admission for an *in-depth* experience three to four weeks after the time of discharge. Such discharge planning promotes trust and acceptance of therapeutic regimes and increases the credibility of the physician.

Patients are usually discharged five to six days after admission and followed by daily phone calls at which time urine tests are reported and insulin dosage



adjusted. Intervals between calls are gradually lengthened as the disease stabilizes, living patterns are resumed and the families become more comfortable with assuming responsibilities. We believe prolonged hospitalization has many detrimental effects upon children, their families and their friends.

### Transition Care

Patients are scheduled to be seen approximately three weeks after discharge. At this time revision of the meal plan is necessary and innumerable questions and concerns about diabetes have begun to accumulate. Most families have begun to accept the disease and have gained enough experience to stimulate their curiosity. They are now willing and anxious to obtain more information. The stage is now set and it is important that physicians recognize that this is the optimal time to provide the patient and his/her family with an in-depth educational program.

The content of such an in-depth program is listed below:

#### OUTLINE OF A DIABETES EDUCATION PROGRAM<sup>7,8</sup>

Introduction, Objectives and Individual Testing  
What is Diabetes? Current and Changing Concepts  
Nutritional Management of Diabetes  
Urine Testing  
Individual Conferences  
Insulin and Oral Agents  
Treatment of Insulin Reactions  
Diet-Exchange System  
Insulin Administration  
Meal Planning During Illness  
Restaurant Planning  
Pattern Control  
Long-Term Problems and Complications  
Adjustment to Diabetes  
Small Groups  
Food Labeling  
Foot Care and Health Measures  
Fat Modification  
Exercise and Its Relationship to Diabetes  
Acute Complications  
Research: New Developments and Hope for the Future  
Course Evaluation and Retesting

It has been our experience that working with families who have been through this educational program is infinitely easier since they have a basic understanding of the disease and an awareness of their own responsibilities in diabetes management which vastly enhances reports and communications. Use of an educational program is an integral part of the therapeutic plan for our patients and these informed families greatly enhance our effectiveness. Patients who are knowledgeable about diabetes are less likely to experience severe insulin reactions and bouts of

diabetic acidosis. In our own practice, we have documented that young patients who have attended our educational program demonstrated better growth patterns than those who have not attended.

### Continuing Education

Several years ago, some of our patients who had excellent initial and in-depth educational experiences were encountering problems with diabetic acidosis. On further investigation, we found that in the intervening three or four years, these children had forgotten some of the basic concepts of prevention, recognition, and treatment of acidosis. We have corrected that problem by now providing a continuing educational experience at each patient visit. We regard each clinic visit as an opportunity to provide patients with an educational experience. Patients always have numerous questions dealing with the immediate problems associated with their diabetes which we are all obligated to answer. It is important, however, to recognize the necessity of updating and reviewing with patients the basic concepts of the disease and its management. Our group has devised an educational flow sheet which includes items such as acidosis, hypoglycemia, urine testing, glucagon administration, insulin injections, the sick day, etc. and it is used as a guide to ascertain that patients keep updated on the basic principles of control and management.

### Acute Problems

The acute problems that confront individuals with juvenile diabetes are hypoglycemia and acidosis. Most episodes of hypoglycemia are mild and informed children can usually detect these episodes and deal with them appropriately. If we are going to make a concerted effort to keep patients in reasonably good control, we expect mild hypoglycemic episodes periodically. These occurrences are usually associated with delayed meals or unusual exercise. It is imperative that all patients be taught how to recognize, treat and prevent such complications. When hypoglycemia goes beyond the mild stages, immediate steps must be taken. It is imperative that other members of the family are prepared to cope with more severe episodes. Patients who are irrational, combative or unconscious can be dealt with if other members of the family are informed. All of our families are instructed in the use of REACTOSE, a glucose containing preparation in a methyl cellulose base which can be administered to those who are unconscious. This is slowly swallowed by reflex action and we have documented a mean blood glucose increment of +31 mg.% 20 minutes after administration.<sup>10</sup>



For the unconscious diabetic, glucagon is an effective substance which can be subcutaneously administered by family members.<sup>11,12</sup>

We recommend all patients have glucagon available and their parents taught to use it appropriately. An effective dosage is 0.025 mg. per kg. up to a total maximum dose of 1 mg. This can be administered subcutaneously with an insulin syringe. Occasionally, after hypoglycemic incidents, we will see patients experience nausea and vomiting for a brief period of time. These episodes appear to be associated more frequently with the administration of glucagon and sometimes may necessitate brief hospitalization. Children given glucagon gradually regain consciousness over a 20 to 30 minute period and then should be fed oral carbohydrates.

The use of 50% D/W intravenously is effective therapy for hypoglycemia; however, it must be given judiciously. Too much glucose over too brief a period may result in hyperosmality with severe consequences. This problem has to be guarded against in children and the problem arises repeatedly among emergency medical services, emergency room personnel and physicians inexperienced with the treatment of diabetes in children. A maximum dose of 25 cc's of 50% D/W should be given to young adults and less amounts to smaller children. All too frequently, 2 or 3 ampules (50 cc's each) of 50% D/W are pumped into these children. Information on hypoglycemia and insulin reactions should be provided to schools and other groups who have responsibility for children with juvenile diabetes. Printed information cards can be obtained from the: American Diabetes Association, 600 Fifth Avenue, New York, New York 10020.

Another severe emergency problem associated with diabetes is acidosis. These patients are usually experiencing abdominal pain, headache, nausea, vomiting and significant dehydration. The most important aspects of the management of juvenile diabetes is to have a treatment plan and then to carefully monitor the blood sugar and electrolyte levels at frequent intervals. Details on therapy are too long to be covered in this article; however, we do routinely repeat blood sugars every two hours and electrolytes every four hours until the patient has shown decided improvement and is reasonably stable. We do not pride ourselves in attempting to restore electrolyte and glucose metabolism in the shortest period of time as we are always concerned about the possibility of cerebral edema with too vigorous therapy. Slow, but steady, improvement of the patient's metabolic state may avoid such problems associated with too rapid a shift of fluids and electrolytes.

A critical time in the course of diabetes in children is when they experience acute illness and particularly gastroenteritis. Frequently, communications by phone with patients may be required at two to four hour intervals. If patients are not readily responding to monitoring at home, they must be seen in the office or emergency room and the appropriate disposition carried out.

Another risk period for these children is during general surgery. One of our patients was recently admitted for elective surgery to a large city hospital without our knowledge and underwent general anesthesia without having a blood glucose determination done until we were contacted post-operatively. Another time a patient's carbohydrate-containing fluid orders were discontinued by the anesthesiologist and the patient underwent surgery with a border line sugar level and no intravenous glucose dripping. On the day of surgery, blood sugars should be drawn on patients early in the morning and again just prior to the surgical procedure. The a.m. insulin dosage should be decreased and supplemental amounts of regular insulin administered throughout the day as indicated by glucose monitoring. If the patient's blood sugar is within reasonable limits, dextrose is dripped at the range of 50 to 100 cc's 10% D/W per hour depending upon the patient's size and glucose levels. The largest danger in anesthesia is hypoglycemia and we prefer our patients to have a blood glucose of 150 and 250 mg.% immediately prior to surgery. At this level, patients are not in danger of diabetic ketosis or acidosis and should not experience hypoglycemia. A repeat blood sugar is obtained midway through the operative procedure if it

TABLE

#### **Suggested Preoperative Orders for Elective Surgery**

1. Patients will be admitted on the day prior to surgery.
2. Blood glucose and urinalysis will be obtained at the time of admission and immediately called to the pediatrician involved.
3. Anesthesiology to be informed that the patient is a diabetic.
4. Patient is to be scheduled as early as possible on the operating room schedule.
5. Blood glucose to be drawn at 6:00 a.m. on the morning of surgery and called to the pediatrician by 7:00 a.m.
6. Pediatrician to determine the patient's insulin dosage.
7. I.V. of 10% Ringer's Lactate to be started on the floor prior to surgery and then rate is to be determined by the pediatrician.
8. Glucose determination and the rate of I.V. during surgery is to be determined by the anesthesiologist. Hypoglycemia is to be avoided.
9. Blood glucose will be obtained immediately upon the patient reaching the post-operative recovery room and results to be called immediately to the pediatrician.
10. Post-operative fluid and insulin orders are the responsibility of the pediatrician.



is prolonged and again immediately post-operative. Suggested admission orders for the management of patients with juvenile diabetes undergoing elective surgery requiring general anesthesia are shown in the Table.

### Long-Term Care

Following attendance of our educational program, patients are usually seen in the office at two to three month intervals depending upon the nature of their disease, its degree of control and their distance from the Clinic. Individual long-range therapeutic plans should be developed and discussed with each family. Consideration for the needs and resources of the individual consumer and provider must be identified and acknowledged. Obviously, the patient who lives long distances away has unique problems as does their local medical resource which may have limited available consultation. Appropriate contingencies will have to be identified and therapeutic plans developed.

Insulin requirements frequently change during the course of the disease. In the early stages of the disease, there is usually some residual islet cell function and reasonable control can be maintained on a single insulin or a single injection of mixed insulins. As the duration of the disease increases, control becomes more difficult and more insulin is usually required. It is frequently necessary to split the dosage and give multiple injections each day. The occasional determination of the fasting blood glucose to assess disease control and evaluate insulin dosage is of limited value in ambulatory patients. Such tests indicate only what the blood sugar is at the time the specific specimen is drawn and do not reflect what the blood sugar might be two hours, two days or two months later. With the frequent "bouncing" of blood sugar levels seen in children, we do not feel that the occasional blood sugar level is a reliable indicator of control and related problems.

Most of our patients over nine or 10 years of age have sufficient knowledge and skill to adjust their own insulin dosages. They are requested to bring their daily urine testing records with them to every clinic visit. It is imperative that physicians look at these tests and assess them not only for frequency of urine testing but also to see that the patients are adjusting their insulin dosages to compensate for alterations in testing patterns. These discussions constitute an important part of the ongoing educational program.

We use the results of 12- and 24-hour urine collections for quantitative glucose determinations to assist us in monitoring our patient population. Patients can be taught to perform these calculations at home

with reasonable accuracy and at minimal costs.

We feel that for reasonable control, patients should not spill more than 5% of their daily carbohydrate intake over a period of 24 hours. For the 10 year old consuming 2,000 Calories a day, this means  $5\% \times 50\% \times 2,000 \text{ Calories} = 50 \text{ Calories}$  or  $50 \text{ Calories} / 4 \text{ Calories per gram} = 12.5 \text{ grams of carbohydrates per day}$ .

These 24-hour collections are collected in four aliquots (breakfast to lunch, lunch to supper, supper to bedtime and bedtime to breakfast). Thus, not only the 24-hour period is evaluated, but if abnormal, the aliquots reveal which time or times of the day are most troublesome. Patient instruction sheets for performing these tests can be obtained by writing the author (DDE).

Rahbar in 1968 reported the presence of an abnormal hemoglobin in patients with diabetes and later identified it as the hemoglobin A<sub>1</sub> component.<sup>13</sup> Trivelli and co-workers also studied this fraction in normal patients and those with diabetes. Among the latter group, it was found that the levels were markedly elevated.<sup>14</sup> Hemoglobin A<sub>1</sub>C is acquired post-translationally and recent studies have suggested that it may be useful in the long-term evaluation and control of diabetes.<sup>15</sup> Normal range of total hemoglobin A<sub>1</sub>, found in our non-diabetic population has been found to be 6.1% to 8.2%.<sup>16</sup> It is thought that the glycosylation process is accelerated in diabetes by the mass action effect of the elevated blood glucose levels. This is regarded as being an irreversible process and since the half life of the average red blood cell is estimated to be 120 days, the degree of elevation of the hemoglobin A<sub>1</sub>C is considered to be a reflection of control over a period of the past 4-6 weeks.<sup>17</sup> Wedness et al<sup>18</sup> recently suggested that a chemically less stable form of the hemoglobin-glucose combination may exist after acute hyperglycemia and warrant overinterpretation of undialyzed hemoglobin A<sub>1</sub>C measurements.

Our own experience with hemoglobin A<sub>1</sub>C has indicated that with the use of hemoglobin A<sub>1</sub>, we could not distinguish between our clinical impressions of patients in fair to good control. The findings in these two groups, however, differed significantly from those under poor control. Consequently, we regard hemoglobin A<sub>1</sub> levels as only one of several parameters that may be used to assess control.

Distinction of the islet cells of the pancreas is usually abrupt but not total. Most children will continue to produce some endogenous insulin for several years after onset of the disease. Since endogenous insulin is somewhat responsive to blood glucose levels, the disease is usually easier to control at its onset. The



gradual loss of the patient's ability to produce insulin can be measured by determining C-peptide measurements in the blood or urine. While of interest, the measurement is of little value in the clinical management of the disease.

Dietary management of juvenile diabetes frequently is difficult to assess since most physicians have little training in this area. Obtaining a good dietary history is time consuming and it is difficult to keep abreast of the content of all of the new foods appearing on the market. Few physicians have a readily available referral source for dietary assistance and few years ago we found that less than 20% of children at the diabetes camp had current realistic diabetic diet plans. Some of these children were teenagers who had not had their diets reviewed since their initial hospitalization several years previously. Fortunately, they were not following their prescribed diets which were several hundreds of calories short of their present needs.

In the management of juvenile diabetes, food should be regarded as a medication and an effective means of controlling blood sugar levels. Insulin lowers blood sugar and the use of food provides us with a means of raising the blood sugar varying amounts at any desired interval. Thus, we do have some control over how often, how rapid and how high glucose rises. All of our patients are on three meals a day plus an afternoon or evening snack. Younger children may require a mid-morning snack. Older children are frequently reluctant to take a snack in a school setting, particularly during the morning hours. We recommend that dietary evaluations be made approximately every two to three months and should be part of the service provided to juvenile diabetics. This can be most efficiently and economically performed by incorporating the skills and knowledge of a trained dietitian. If these services are not immediately available in a practice setting, then community resources should be sought and integrated into the plan for continuity in health care.

It is important that at each clinic visit, the growth and development of these children be assessed. Inadequate control is quickly reflected in a leveling off of weight and height. Failure to increase in height at the usual rate is usually preceded by a three to six month fall-off in weight. Monitoring the numerous facets of control of these children is important and physicians who do not have or wish to develop comprehensive care may wish to supplement their individual services by arranging for periodic visits to a subspecialty clinic.

### **The Brittle Diabetic**

Brittle diabetes does occur. Most frequently,

however, it is of psychological origin and is a result of behavioral problems. Almost without exception, the children who are constant repeaters in the hospital have underlying behavioral problems.

Overinsulinization is another culprit to be ruled out in the child who is difficult to control. In 1959, Somogyi<sup>19,20</sup> reported a rebound phenomena frequently observed in children. When too much insulin is administered, the resulting hypoglycemia is thought to trigger the adrenal gland and a burst of catecholamines are released. This invokes a responsive release of liver glucose which, in turn, grossly elevates the blood sugar and increases glucosuria. The resulting glucosuria is then misinterpreted and additional insulin is added to the patient's therapeutic regime and the cycle starts over again. The Somogyi effect is to be guarded against. The usual range of insulin required is 0.5 to 1.0 units per kg. Requirements above this level should be suspect for overinsulinization.

### **Team Care**

The prevalence of diabetes in the State of Minnesota is only one out of every 529 school-aged children and consequently most physicians and pediatricians may have only one or two patients in their entire practice.<sup>21</sup> Such small numbers make it difficult to establish or maintain an in-depth management program and the necessary ancillary personnel. Teams providing care to juvenile diabetics optimally should consist of a physician familiar with the disease, a nutritionist, a nurse and the availability of counseling services. The latter is particularly important in juvenile diabetics who have marked predilection for rebellion not only against the usual teenage problems but also against their disease.<sup>22</sup> Diabetes is a very effective tool frequently used to manipulate family members, schools and medical personnel. We now ask a family counselor to see all of our newly-diagnosed patients at the time of admission and thus take a prophylactic approach in assisting these families to accept the disease and the demands it makes.

When diabetes specialty teams are working in a planned program of care, every effort should be made to maintain close communications with local physicians and those who see these patients for primary care problems. In times of significant stress, phone contact between local physicians and specialists is encouraged.

### **The Future**

Control of diabetes has always been linked to and evaluated by assessing blood glucose levels. We know, however, that when carbohydrate metabolism is



disturbed, there is simultaneously an alteration in the body's fat and protein metabolism. The nature and extent which these alterations are influential in the development of these complications has not been well identified. Attempts to control blood sugar at the present time are relatively primitive. There can be no doubt that insulin per se is an effective drug. Our primary difficulty at this time, however, is the delivery of insulin in a physiological manner.

Currently, the use of mixtures of insulin are common as is the technique of "splitting" the dosage and giving two or more injections each day but such techniques have not solved the problem. A recent paper suggests that insulins attached to maltose which, in turn, are bound to a larger molecule might be released in response to alterations in blood glucose and hopefully might make the insulin depot responsive to the level of blood sugar.<sup>23</sup>

Instrumentation capable of assessing blood glucose levels in the home setting has been introduced into the therapeutic realm and its use encouraged among the general diabetic population in order that they might juggle their insulin diet and exercise to attain stability. Multiple determinations of blood sugar throughout the day and night have been shown to be of great assistance in evaluating control and permits the patient to respond accordingly.<sup>3-6</sup>

Simultaneously, large complex instruments complete with sensors and a computer, are capable of monitoring blood sugar throughout the 24-hour period and infusing insulin and glucose according to the individual patient's needs. Such machines are expensive, large, complex and require the attendance of a

technician; thus, they are effective but are impractical for daily use.

More recently, investigators have reported the use of preprogrammed insulin delivery systems in which insulin is administered subcutaneously with portable infusion devices.<sup>24,25</sup> This permits the frequent intermittent subcutaneous delivery of small amount of insulin with periodic large boluses being delivered when carbohydrate consumption increases. These reports have been encouraging and are of considerable interest. Tamborlane and Felig reported among a group of seven children studied for two to four days on an infusion pump that their mean hourly plasma glucose could be controlled at  $105 \pm 5$  mg.% in contrast to a mean of  $237 \pm 28$  mg.% when managed by conventional means.<sup>26</sup> The Yale group published their findings following a 3 to 8 month experimental period which indicates that these pumps are effective and can be tolerated by ambulatory patients.

Pancreas or islet cell transplantation has been demonstrated to be successful among highly inbred strains of rats. Its usage in humans has been experimental and with minimal success. Promises for the future, however, are encouraging as increased knowledge about the immune barrier is gained.

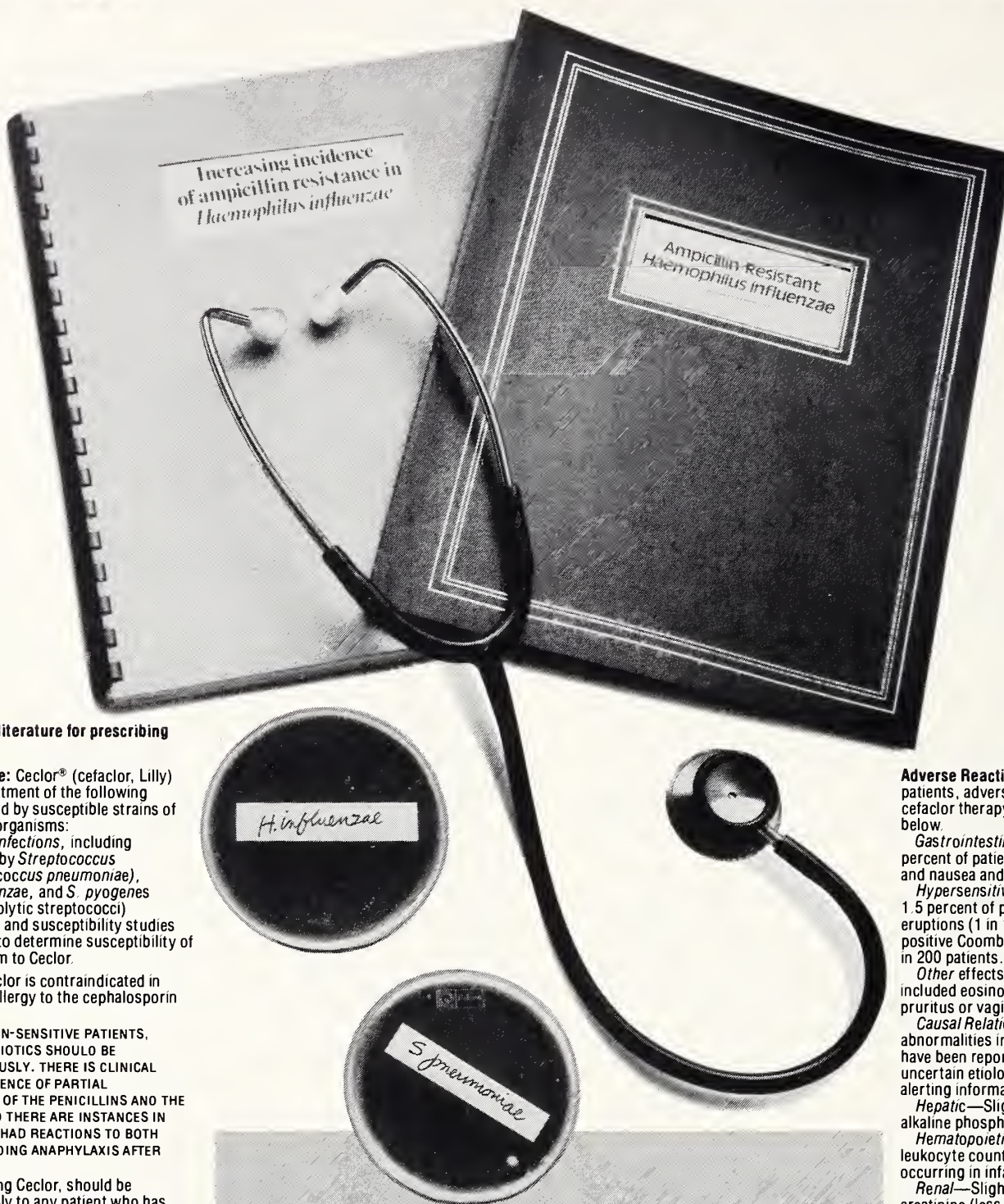
In summary, diabetes in children is a serious chronic disease which requires a comprehensive planned approach to management by a group of knowledgeable health care professionals who are working cooperatively with informed patients and their family members. The hopes for the future are bright, but in the interim, it is imperative that increased emphasis and efforts are made to achieve control.

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# An added complication... in the treatment of bacterial bronchitis\*



**Brief Summary.**  
Consult the package literature for prescribing information.

**Indications and Usage:** Ceclor® (cefactor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

*Lower respiratory infections*, including pneumonia caused by *Streptococcus pneumoniae* (*Diplococcus pneumoniae*), *Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci)

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

**Contraindication:** Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

**Warnings:** IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS TO BOTH DRUG CLASSES (INCLUDING ANAPHYLAXIS AFTER PARENTERAL USE).

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

**Precautions:** If an allergic reaction to cefactor occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of cefactor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such a condition, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

**Usage in Pregnancy**—Although no teratogenic or antifertility effects were seen in reproduction studies in mice and rats receiving up to 12 times the maximum human dose or in ferrets given three times the maximum human dose, the safety of this drug for use in human pregnancy has not been established. The benefits of the drug in pregnant women should be weighed against a possible risk to the fetus.

**Usage in Infancy**—Safety of this product for use in infants less than one month of age has not been established.

**Adverse Reactions:** In clinical studies in 1493 patients, adverse effects considered related to cefactor therapy were uncommon and are listed below.

*Gastrointestinal* symptoms occurred in about 2.5 percent of patients and included diarrhea (1 in 70) and nausea and vomiting (1 in 90).

*Hypersensitivity* reactions were reported in about 1.5 percent of patients and included morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs tests each occurred in less than 1 in 200 patients.

*Other effects* considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

*Causal Relationship Uncertain*—Transitory abnormalities in clinical laboratory tests results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

*Hepatic*—Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

*Hematopoietic*—Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

*Renal*—Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[070379R]

**Some ampicillin-resistant strains of *Haemophilus influenzae*—a recognized complication of bacterial bronchitis\*—are sensitive to treatment with Ceclor.<sup>1-6</sup>**

In clinical trials, patients with bacterial bronchitis due to susceptible strains of *Streptococcus pneumoniae*, *H. influenzae*, *S. pyogenes* (group A beta-hemolytic streptococci), or multiple organisms achieved a satisfactory clinical response with Ceclor.<sup>7</sup>

# Ceclor®

## cefactor

Pulvules®, 250 and 500 mg

\* Many authorities attribute acute infectious exacerbation of chronic bronchitis to either *S. pneumoniae* or *H. influenzae*.<sup>8</sup>

**Note:** Ceclor® (cefactor) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

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# Childhood Irradiation and the Incidence of Thyroid Cancer

ALVIN L. SCHULTZ, M.D.\*

**Following childhood neck irradiation, there is a 30 fold increase in the incidence of thyroid carcinoma and a five fold increase in benign thyroid adenomas. All physicians should try to identify these patients in their practice, and those with thyroid nodularity should have surgical thyroidectomy.**

**I**N 1950, DUFFY and Fitzgerald<sup>1</sup> suggested a relationship between low dose x-ray therapy to the head and neck during childhood, and the subsequent occurrence of carcinoma of the thyroid gland. Between 1950 and 1960, a number of other reports<sup>2-5</sup> appeared, proposing such a relationship, however, almost nothing was done to alert either physicians or the public. X-ray exposure of the head and neck regions during infancy and childhood for thymus and tonsillar enlargement, cervical adenopathy and acne, continued to be widely used into the 1960's. Between 1968 and 1976, many more studies,<sup>6-10</sup> several of which surveyed large populations who had received head and neck irradiation during childhood, reported an alarmingly high incidence of thyroid carcinoma appearing during adult life. As a result, nationwide interest was aroused and continues to the present time. The significance of these reports, the implied public health hazard, and the management of the problem remains controversial and this is reflected in a recent editorial by Crile, Esselstyn and Hawk.<sup>†</sup>

In the discussion which follows I will present some of the evidence which has led to the concept that a casual relationship exists between head and neck irradiation and the development of thyroid cancer, and I will offer recommendations for the management of this problem.

## Evidence

Duffy and Fitzgerald<sup>1</sup> reviewed 28 cases of childhood thyroid cancer and found that nine (32%)

had had irradiation of the thymus gland between four and eighteen months of age. Clark<sup>2</sup> reported a group of 15 children with thyroid carcinoma, all of whom had had low voltage irradiation to the neck and chest previously.

De Groot and Paloyan<sup>8</sup> reported 50 sequentially admitted patients with thyroid carcinoma whom they treated between 1968 and 1972. Among the 30 patients who had not received head or neck irradiation previously, there were 21 women and nine men and the mean age was 42 years at the time of diagnosis of thyroid cancer. There were 21 papillary, follicular, or mixed carcinomas with one death, and eight poorly differentiated or anaplastic cancers with four deaths. In contrast, among the 20 patients who had received head or neck irradiation, there were 13 males and seven females, and a mean age of 28 years at the time of diagnosis. There was an average of 20 years between the x-ray exposure and the appearance of a neoplasm. There were 5 papillary, one follicular, nine mixed, and no undifferentiated or anaplastic carcinomas. There was one death in a patient with a mixed papillary/follicular carcinoma. The reasons for the childhood irradiation (estimated to be 400-900 rads) in these patients were thymus enlargement, tonsillitis, acne, and impetigo.

Refetoff and associates<sup>9</sup> examined 100 persons with a history of low voltage X-ray irradiation to the neck and found 26 to have a palpable thyroid gland abnormality. Surgical thyroidectomy was recommended in 18 of the 26 and, among the 15 who were operated upon, seven were found to have thyroid cancer and eight had benign adenomas. The carcinomas were papillary, follicular, or mixed. Five of the cancers had metastasized to regional nodes or had invasion through the capsule or into blood vessels. The

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mean age at the time of operation was 29 years, an average of 24 years after the neck irradiation. The incidence of thyroid neoplasms was the same among males and females.

Favus et al.<sup>10</sup> examined 1056 of 5266 persons who had received head or neck irradiation therapy for benign conditions during childhood at Michael Reese Hospital, Chicago between 1939 and 1962. Thyroid nodules were found in 27%, and among 182 persons operated upon, 60 (33%) were found to have papillary, follicular or mixed thyroid cancer. Benign adenomas were also found in three-fourths of the thyroid glands containing carcinoma. None had distant metastasis, but local invasion and regional node metastasis was common. The finding of an abnormal thyroid scintigram without a palpable abnormality was frequent, and in 25% of these a carcinoma was found at operation. Nearly one-half of the carcinomas had multicentric foci of tumor in both lobes. The incidence of thyroid cancer was about equal among men and women, and the mean age at the time of operation was 32 years.

Swelstad et al.<sup>11</sup> reported the results of thyroidectomy in 125 patients with a history of irradiation to the head or neck during childhood and the subsequent development of a palpable thyroid mass during adult life. Papillary, follicular, or mixed thyroid cancers were found in 42 (34%), and nine (20%) had metastases to regional nodes. Almost one-half of the tumors were less than 1 cm in greatest diameter, 40% had multicentric cancer foci, and associated benign adenomas were commonly found.

Schneider, and Associates<sup>12</sup> have reported an increased occurrence of benign and malignant salivary gland and parotid gland tumors in persons who have had childhood irradiation to the nasopharyngeal/tonsillar region.

There have been numerous other studies reported of an increased incidence of thyroid cancer following childhood head and neck irradiation for benign conditions. The time of x-ray exposure varies from infancy to adolescence. Many of the studies are open to criticism because they are retrospective and uncontrolled. The natural history of small asymptomatic papillary thyroid carcinomas is not well understood, nor is the significance of multicentric microscopic foci of carcinoma in other parts of the thyroid gland understood.

### Controversy

It has been argued that the type of thyroid tumor associated with irradiation, namely papillary, rarely

results in the death of the patient. In a group of 307 patients with papillary thyroid carcinoma followed up to 34 years, Crile<sup>13</sup> reported that less than 1% of those who had been irradiated died of thyroid cancer. If the mortality from papillary thyroid cancer is so low, can the recommended radical thyroid surgery and the massive expensive nationwide case finding effort be justified?

The incidence of small (< 1.5 cm) unsuspected, so-called "occult" cancers, found at the time of thyroidectomy, is particularly high among irradiated patients. "Occult" papillary thyroid carcinoma is considered by many to be a harmless lesion without clinical significance or mortality.<sup>10,11,14,15</sup> Fifty-eight patients with "occult" papillary thyroid cancer and regional nodal metastases were followed for three to 30 years at the Mayo Clinic, and none were dead due to the thyroid cancer<sup>15</sup>. In an additional 82 patients without regional node metastasis at the time of surgery followed two to 30 years, none had had a recurrence nor local or distant metastasis of the cancer. However, among patients with papillary thyroid cancer and distant metastases, the mortality due to the cancer has been reported to be 15-20 percent, and among patients with metastatic follicular thyroid carcinoma the mortality may be as high as 50 percent.<sup>16,17</sup>

Another issue which is still being argued relates to the extent of the surgery (total vs subtotal thyroidectomy) to be performed in patients with small primary papillary carcinomas and multicentric foci of microscopic tumor in both lobes.

Mazzaferri and associates,<sup>18</sup> in a study of 576 patients with papillary thyroid cancer, reported twice as many recurrences and a greater number of deaths following subtotal thyroidectomy than when total thyroidectomy was the operation performed. However, following total thyroidectomy 10% of the patients had permanent hypoparathyroidism. Harness et al.<sup>16</sup> reported only 4% permanent hypoparathyroidism and laryngeal nerve injury in a series of 252 patients who underwent total thyroidectomy at the University of Michigan. Others have reported permanent hypoparathyroidism in as high as 50% of cases after total thyroidectomy. In 328 patients with papillary thyroid carcinoma treated surgically at the Mayo Clinic, unsuspected multicentric foci of carcinoma, involving both lobes, were found in 20% of the cases. However, because of the high incidence of permanent hypoparathyroidism, subtotal thyroidectomy leaving a remnant of one lobe was recommended, and total thyroidectomy was done only if extensive and marked multicentricity of tumor was present.<sup>19</sup>



Paloyan and associates<sup>20</sup> reported the results of total thyroidectomy in 70 patients with thyroid nodules following childhood x-ray exposure. Fifty-four percent had papillary, follicular, or mixed thyroid carcinoma, more than half had regional node metastases, four had distant metastases, and there were multicentric foci of tumor in both lobes, in 45%. At surgery the parathyroid glands were identified, minced into fine pieces, and implanted in the sternocleidomastoid muscle. One patient developed permanent unilateral recurrent nerve palsy. Nineteen patients (17%) had temporary tetany following surgery but only two (3%) had permanent hypoparathyroidism.

### Conclusions

The weight of evidence which has accumulated over the past 25 years supports the concept that childhood irradiation of the neck is associated with a greatly increased incidence of thyroid carcinoma in later life. The length of time from the x-ray exposure to the appearance of a clinical thyroid mass varies from five to 35 years. In an irradiated population, the probability of developing a thyroid carcinoma appears to be about 7%. The probability of thyroid carcinoma developing in an irradiated person is approximately 30 times greater than in a non irradiated person. Benign thyroid adenomas are about five times more common in an irradiated population.

The malignant thyroid lesions found in irradiated persons have been mainly papillary or mixed papillary-follicular adenocarcinoma, however about 25% of the tumors are follicular adenocarcinomas and carry a greater risk of distant metastasis. No undifferentiated, anaplastic, or other highly malignant thyroid carcinomas have been reported. About half of the thyroid carcinomas will be of the "occult" papillary type (less than 1.5 cm in diameter) and are not the palpable thyroid mass which lead to operation. Between 40 and 50% of irradiated patients with thyroid cancer will have multicentric microscopic foci of carcinoma in both thyroid lobes, and one third or more will have carcinoma in the regional cervical lymph nodes.

The mean age of irradiated patients, when the thyroid carcinoma is discovered, will be between 29 and 32 years, and the x-ray exposure to the thyroid region will usually have been between 250 and 400 rads, although smaller x-ray exposures associated with development of thyroid malignancy have been reported. In contrast to thyroid carcinoma in non irradiated persons, which is about three times more frequent in

women, these thyroid cancers occur with about equal frequency among men and women. So far, the number of deaths directly attributed to the irradiation related thyroid cancer has been few. However, despite the known slow rate of growth of papillary carcinoma of the thyroid, the great frequency of regional node involvement at the time of original surgery, the youth of the patients, and the frequency of follicular carcinoma suggest that with time the mortality rate may be considerably higher than now reported.

### Recommendations

A general consensus has been reached among endocrinologists and other scientists interested in this problem in regard to case finding among the irradiated population and the management of irradiated persons once identified. This consensus is reflected in the discussion and recommendations developed at a National Institutes of Health workshop held September 24-25, 1975.\*

The following are my recommendations which, in general, do not deviate significantly from those developed at the NIH workshop:

1. X-ray irradiation of the neck and thyroid region for benign conditions during childhood was a common practice between 1930 and 1960 and hundreds of thousands of children were irradiated. About 25 percent of this population are likely to develop thyroid nodules and about 40 percent of these nodules will be malignant. Thus it is in the public interest that all physicians attempt to identify these persons among their patients. The question, "*Have you ever had x-ray therapy to your head, neck, or upper chest,*" should be a standard part of every history."
2. *Those patients with a history of head and neck irradiation, should have a careful examination of their thyroid, parotid, and submaxillary glands looking for the presence of nodularity or other abnormality.*
3. If no thyroid nodularity is found, these patients should be followed with a *careful thyroid and salivary gland examination each year, thereafter.* The patients should also be instructed in self examination by inspection and palpation, and the reasons for careful followup explained.
4. If a thyroid nodule or nodules are found in a patient who has had prior irradiation of the neck region, *surgical thyroidectomy should be strongly recommended.* Total thyroidectomy with implantation of

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minced parathyroid gland into muscle tissue is probably the operation of choice in the hands of an experienced head and neck surgeon. The least that should be done is a radical subtotal thyroidectomy leaving a remnant of the thyroid lobe on the contralateral side from the palpable nodule. Removal of cervical lymph nodes on the side of the carcinoma by means of a modified neck dissection is also reasonable. I take a rather aggressive approach to this problem because these patients are usually young adults who otherwise have a long life expectancy, and perhaps one-third will have a predominantly follicular thyroid cancer which carries a mortality of 25 percent or more if not cured by the initial surgery. Although papillary thyroid carcinoma is very slow growing and is much less a threat to life, recurrence of papillary carcinoma may be associated with considerable morbidity, discomfort, and expense to the patient. A cure of the thyroid carcinoma should be attempted, by all reasonable means, at the time of the original operation.

5. All patients with thyroid carcinoma, following surgery, should be placed on *suppressive dosage of thyroid hormone, which should be continued the rest of their lives*. I also recommend that all patients with a history of head and neck irradiation, whether a thyroid neoplasm is found or not, be placed on suppressive thyroid hormone therapy. I use *l*-thyroxine, 150  $\mu$ gm once daily, for this purpose.
6. I usually obtain a thyroid<sup>123</sup> I scintigram in these

patients at the time of initial examination and/or prior to surgical thyroidectomy. However, *I do not recommend that the thyroid scintigram be used as the basis for deciding whether surgery should be done*. In a patient with a history of neck irradiation, "hot" (hyperfunctioning) nodules on the thyroid scintigram should be removed surgically.

7. In irradiated persons with diffuse thyroid gland enlargement I recommend thyroid hormone suppression and continued observation, unless neoplasm is suspected on the basis of other findings.
8. *I do not recommend needle biopsy of thyroid nodules in irradiated persons*, since multicentric foci of carcinoma are so common in these patients, and negative needle biopsy should not be the basis for recommending observation rather than surgery.
9. *I do not recommend surgical thyroidectomy on the basis of an abnormal thyroid scintigram in the absence of a clinically palpable thyroid mass*, however, these patients should be more closely observed at more frequent intervals.

The dangers of head and neck irradiation during childhood, adolescence, and adult life for benign conditions such as tonsillar or lymph node enlargement, acne, thymic enlargement, and thyroiditis, are now well known, and it can be assumed that the irradiated population at risk will not be increased in the future; however, with the large numbers exposed, as recently as 1960, the observation and search for thyroid neoplasms in this population should be continued another 40-50 years.

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# Artificial Insemination Utilizing Donor Semen

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Insemination utilizing donor semen is an effective method for the treatment of infertility due to oligospermia or azoospermia. AID is also performed to minimize or obviate known genetic risk factors. The major complication is bacterial salpingitis which is particularly likely to occur in women with pre-existing tubal damage. The procedure was analyzed in our initial 124 couples. In our experience to date, only one major anomaly has been observed among over 250 offsprings.

**I**NSEMINATION UTILIZING donor semen has been enthusiastically accepted as effective treatment for infertility attributed to the male, often in preference to the alternative of adoption. A program for performing AID was instituted at the University of Minnesota in 1971. We initially analyzed the indications for performing the procedure, the techniques utilized, and the results of treatment in 124 couples. The service was subsequently expanded, and presently more than 250 children who were conceived by AID have been delivered.

AID is usually performed for azoospermia and oligospermia (Table 1). Sterility can be equated only with complete absence of motile sperm. Azoospermia

TABLE 1

Indications for AID

Azoospermia	93
Oligospermia	26
Other	5
Total Males	124

was present in 93 of 124 males. The various etiologies included vasectomy, congenital absence of the vas deferens, undescended testes, hypoplastic testes, mumps orchitis, and tuberculous and gonococcal epididymitis. Reduced fertility potential and therefore oligospermia is defined as persistent production of less than 20 million motile semen with normal morphology per ejaculate. Rare pregnancies have occurred with less than 5 million motile semen per ejaculate. In

infertility due to oligospermia, reported pregnancy rates are 15 to 19%, and pregnancy rates are not increased by performing artificial insemination with the husband's semen (AIH). Oligospermia was present in 26 of 124 males; although 6 had recognized causes, 20 were of idiopathic origin. AID is also performed for genetic indications such as blood group incompatibility which has resulted in erythroblastosis fetalis, or other known genetic risk factors which the couple wish to minimize or obviate. AID is contraindicated when pregnancy would entail a significant risk to the mother.

Our goal is to place the child in a physically and psychologically healthy family with parents having a life expectancy of at least twenty years. The initial assessment of the couple desiring AID includes documentation of the deficiency in semen quality. The psychologic status of the couple is assessed during the interview. A comprehensive general medical history is obtained from the woman and she is given a complete physical examination. Thyroid function studies consisting of assays of circulating TSH and free thyroxine are routinely obtained. The prospective recipient is further evaluated for disorders of ovulation and anatomic defects. Apparent ovulation is assessed from basal body temperatures. BBT's are subsequently utilized for timing inseminations. The anatomy of the uterine cavity and fallopian tubes is routinely assessed with a hysterosalpingogram (HSG). In addition, laparoscopy is performed: (1) prior to beginning AID if the initial evaluation or HSG suggests defects or (2) if pregnancy is not achieved after completing six cycles of well-timed inseminations; utilizing these criteria 65 of 124 women did not require laparoscopy. Of those patients who had laparoscopy performed, the procedure revealed or verified the presence of disease which

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impaired fertility potential in 61% of the patients with abnormalities determined by the initial physical examination or HSG, and 57% of the patients who failed to become pregnant after six cycles of AID.

Of the initial 124 females, only 48 (39%) had fertility potential which was assessed as being normal (Table 2). Seventy-six (61%) had one or more defects which would impair fertility potential; 62 exhibited anatomic abnormalities of the cervix, uterus, tubes, or pelvis and 22 women had defects of ovulation. Thus, in the couple referred for the correction of an obvious defect in male fertility potential, nearly two-thirds of the women had some abnormality which would contribute to infertility.

TABLE 2

Fertility Status of AID Recipient		
Normal	48	39%
Impaired	76	61%
Anatomic defect	62	
Ovulatory dysfunction	22	

During the initial interview, the couple is informed of the likelihood of success and the potential adverse effects of AID. In the original 124 females, the pregnancy rate was 13% per cycle; of those who continued through six cycles of insemination, 70% achieved pregnancy. The 19% incidence of spontaneous abortion in this group did not differ significantly from the rate reported in the general population. At the present time, more than 250 infants have been delivered. Only one child was reported to have a hereditary or developmental defect. This infant had Mongolism due to a 21 trisomy; neither the mother nor the donor was a translocation carrier (Table 3). It has been suggested that the high percentage of normal offspring resulting from AID represents a program of positive eugenics.

Potential complications are discussed and enumerated in the informed consent document. The most common adverse effect of AID is salpingitis, chemical or bacterial. Chemical salpingitis is due to direct peritoneal spill of semen resulting from the injection of an excessive volume of semen into the cervical canal; it is characterized by immediate pelvic pain which subsides within minutes to hours. Bacterial salpingitis occurred on two occasions following a total of 1377 inseminations performed during the years prior to 1976. As a result of this complication, we cultured 97 consecutive donor semens from the collection container utilizing a method which excluded anaerobes and gonococci. Only 10 semen specimens failed to grow organisms. Two or three organisms were cultured from most specimens. Potentially virulent

organisms including Group B  $\beta$ -Streptococcus, coagulase-positive Staphylococcus and Escherichia coli were cultured in 10% of the specimens. Currently, each donor specimen is cultured for the gonococcus at the time of the insemination, and results are reported within 24 hours. In the 2100 semens utilized since 1976, the gonococcus was cultured from only one semen specimen; the female recipient was asymptomatic prior to initiating antibiotic therapy and did not develop clinical disease. Because bacteria with the potential to produce disease are introduced at each insemination, we have made a concerted effort to exclude patients with pre-existing tubal damage prior to initiating AID. Despite aggressive interpretation of the hysterosalpingogram and liberal utilization of laparoscopy to exclude pre-existing tubal damage, one additional instance of non-gonococcal bacterial salpingitis has occurred since 1976.

In addition to enumerating the potential complications, the informed consent outlines the responsibilities of the couple as future parents: "It is further agreed that from the moment of conception the husband hereby accepts the act as his own, and agrees: (a). That such child or children so produced are his own legitimate child or children and are the heirs of his body, and (b). That he hereby completely waives forever any right which he might have to disclaim such child or children as his own, and (c). That such child or children so produced are, and shall be considered to be, in all respects including descent of property, child or children of his body."

TABLE 3

## Pregnancy in 124 AID Recipients

	Rate
Success per cycle	13%
Spontaneous abortion	19%
Major Infant Anomalies <	1%

The donors have always been predominantly medical students or physicians. These men are preferable as donors because of their: (1) documented above-average intelligence, (2) ability to provide a valid genetic history, and (3) awareness of the need for confidentiality. The quality of the donor semen must be optimal but documentation of fertility is not required. The donor's blood type is obtained and his VDRL is obtained to screen for syphilis. When genetic indications exist, appropriate additional screening is preferred. Recently, we have been requiring the donors to sign a waiver in which they relinquish any claim to or jurisdiction over the offspring which result from artificial insemination. Recipients may request donor characteristics in addition to body-build and skin, hair,



and eye color. To respond to these requests, we are now tabulating donor participation in art, music, athletics and religion.

The procedure of donor insemination is performed six days of the week. The couple is advised to discontinue the use of douches and spermicidal lubricants such as KY jelly during the cycles in which AID is performed. The coordinator receives the donor semen at a site located away from the AID clinic. Inseminations are performed by physicians in gynecological specialty training who are supervised by the staff reproductive endocrinologists. The timing of apparent ovulation is deduced from the days of highest frequency in previous cycles, and usually two to four

inseminations are planned on alternate days to span this interval. Ovulation-inducing agents such as Clomid are utilized for disorders of ovulation only. In a paired study of AID recipients with regular ovulatory cycles we found that treatment with Clomid did not increase the pregnancy rate.

The results of the AID program have been immensely gratifying. The parents are delighted with their healthy children.

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OBSTETRICIAN-GYNECOLOGIST with special interest in gynecological surgery wanted to join established multi-specialty group in northern Minnesota. Growing community, excellent hospital facilities, year round recreation area. Contact C. J. Johnson, M.D. or Brad Smith, Administrator; Grand Rapids Clinic, P.A., Grand Rapids, Minnesota 55744, 1-218-326-9482.

(Continued to Page 544)



# Rheumatology Corner

## Arthritis and Diabetes

ROGER S. COLTON, M.D.

**D**IABETICS ARE predisposed to arthritic manifestations as sequelae to their metabolic and vascular abnormalities. A resume of arthritic syndromes in diabetes follows:

### Joint and Soft Tissue Contractures and Limitations

Finger joint contractures, particularly of the PIP joints, but also the wrists, elbows, ankles, and toes may occur in juvenile diabetics caused by periarticular and dermal thickening associated with capillary basement membrane abnormalities. Soft tissue thickening causes modest limitation and does not strikingly interfere with activity. Middle-aged diabetics are predisposed to Dupuytren's contractures and associated fascial thickening with or without flexion tendon contractures of the fingers. Periarthritis of the shoulders, frequently bilateral, appears to be more prevalent in diabetics as a result of vascular compromise of the rotator cuffs. Complications of periarthritis can be a vasomotor-induced shoulder-hand syndrome.

### Gout and Pseudogout

Glucose intolerance appears to be increased in gouty individuals, but whether diabetics have a higher instance of hyperuricemia is debatable. Obesity appears to be the most striking conjoined metabolic abnormality associated with hyperuricemia, gout, and diabetes mellitus. Forty to sixty percent of individuals with documented pseudogout have diabetes mellitus. Shedding of calcium pyrophosphate crystals into synovial fluid by degenerating cartilage is an age-related process as in adult-onset diabetes mellitus. Gout and pseudogout can occur concomitantly in the same individual and has been reported in diabetics.

### Septic Joint

Septic joint disease is seen commonly today in individuals who have compromised immunologic mechanisms. Diminished leukocyte mobilization, phagocytic activity, and bacterial killing have been noted in diabetic individuals. This predisposes the diabetic to septic joints, frequently nosocomial organisms such as gram negative and staphylococcal infections. Septic joint must be ruled out particularly in a setting of an acute monoarticular arthritis in a

diabetic.

### Neuropathic Joints

The most common cause of a neuropathic joint (Charcot's joint) today is the diabetic with sensory deprivation of the forefoot. Smoldering infection in the diabetic may also predispose to unilateral painless destruction and disorganization of the subtalar and tarsal joints. Less often, ankles, wrists, and fingers may have similar changes if sensory deprivation occurs. Radiologic ankylosing of the cervical and lumbar vertebra is said to be more common in diabetes and attributed to atypical neurotropic phenomenon. More likely this represents a predisposition of diabetics to diffuse idiopathic skeletal hyperostosis (DISH).

### "Bronze" Diabetes

Hemochromatosis may induce diabetes mellitus as well as an accelerated arthropathy presenting with an atypical presentation of degenerative disease of the PIP joints of the hands. The PIP joints are unusual joints for idiopathic degenerative arthrosis and may be an early finding suggesting the diagnosis of hemochromatosis. Chondrocalcinosis is also common in hemochromatic individuals, and both chondrocalcinosis and hemochromatosis may be a significant factor in this atypical location for this degenerative joint disease.

### Arthritis Drugs and Diabetes Mellitus

Treatment programs for diabetic arthritics may have significant drug interreactions. Historically salicylates were one of the earliest medications used for attempting to lower blood sugar. High dose salicylate therapy increases utilization of peripheral tissue glucose and blocks gluconeogenesis. It may also predispose, by a renal mechanism, to potassium depletion.

Salicylates can be effectively used in treatment of arthritis in diabetics if awareness of the potential hypoglycemic effect is considered. Other non-steroidal anti-inflammatory agents such as indomethacin, phenylbutazone, ibuprofen, fenoprofen calcium and naproxen compete with protein binding sites with the oral hypoglycemic agents, thereby increasing the pharmacologic properties of the hypoglycemic agents. These drugs can be used in the presence of oral hypoglycemics if an unchanging dosage of both drugs is prescribed and blood sugars monitored regularly.



## Classified Advertisements

(Continued from page 542)

WANTED: One or two primary care physicians to assume an incorporated, well established practice in rapidly developing area at the edge of downtown Minneapolis Hospital within walking distance of office. Available Aug. 1, 1980. Write Minnesota Medicine, (559) 101 E. 5th St., St. Paul 55101.

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MEDICAL DIRECTOR For Non-Profit Women's Health Service in Minneapolis, Minnesota, being sought to direct its gynecology and abortion services. OB-GYN specialist preferred. Responsibilities include supervision of medical personnel, general gynecology and contraception; experience in vacuum aspiration technique required. Must be sensitive to women's health issues. Salary negotiable depending upon qualifications and experience. Medical malpractice provided. Contact Renee Ward or Robert McCoy, Midwest Health Center for Women, 825 South 8th Street, Suite 1012, Minneapolis, Minnesota 55404 (612) 332-2311.

SOUTHWESTERN MINNESOTA RURAL primary care group — 12 physicians (8 Family Physicians, Internist, 2 General Surgeons, Pediatrician) in an Agricultural-Commercial-University town of 12,000+ invites board eligible/board certified Family Physician and OB/GYN Physician to join progressive patient-oriented practice in a 75 bed new hospital and ambulatory care center. USUAL CHAMBER OF COMMERCE CLAIMS NEARLY TRUE HERE! Contact C.P. Martin, M.D., Doctors' Plaza, P.A., Marshall, MN 56258, Phone 507-532-9631.

ALLERGY specialty position available with Mankato Clinic, Ltd. Our 30 man multi-specialty group attracts specialty referrals from a southern Minnesota area of 200,000 population. Excellent group practice opportunity in All-American community with full hospital services; full range of group fringe benefits; liberal time off; salary first year; incentive pay thereafter. For more information call collect R. F. Roskens, Administrator, or Dr. B. C. McGregor, 507-625-1811.

GENERAL SURGEON NEEDED to replace present surgeon who is retiring from private practice July 1, 1980 in a seven member primary care group serving a large area of South Central Minnesota and North Central Iowa located in the City of Blue Earth, Minnesota which is small-rural with a stable economy related to agriculture and small industry. Our offer is \$60,000.00 salary with an incentive bonus for one year with offer of full membership after one year. Contact John W. Anderson, M.D., Blue Earth Medical Center, Ltd., Blue Earth, MN 56013, (507) 526-2171.

WE ARE LOOKING for a GENERAL PRACTITIONER to work in Occupational Medicine and the Emergency Room at the Mankato Clinic, Ltd. For more information call collect R. F. Roskens, Administrator, or Dr. B. C. McGregor, 507-625-1811.

WANTED: FP to join 3 man group at Southdale Med. Bldg., suburban Mpls. Hospital adjacent. Practice growth opportunity, as senior partner wants to cut down his hours. Contact Kenneth V. Hodges, M.D., B-20 Southdale Medical Building, Minneapolis, Minnesota 55435.



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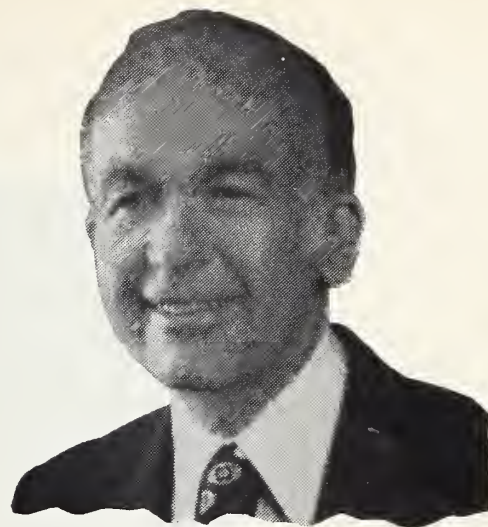
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# President's Letter



## Twin Cities Veterans Administration Hospital

By the time you read this, the fate of Congressman Martin Sabo's rider to the Veterans Administration Appropriation Bill, limiting the size of the new Veterans Administration Hospital, will very likely have been voted up or down by the House of Representatives.

If it remains attached to the bill, it will represent a triumph for responsible health planning. Even if it does not, it represents an opportunity to dramatically demonstrate the difference in what the federal government requires of the private sector regarding excess beds, duplication of specialized facilities and utilization, and what it asks of its own medical institutions.

Federal hospitals are not subject to utilization review and health planning in the way that non-federal hospitals are. Most who have had experience in and with federal medical institutions would agree that they would profit by such review and planning.

The House of Delegates of the Minnesota Medical Association at its May 1980 session adopted a resolution that the Association take appropriate action to attempt to assure that the proposed development of a new Veterans Administration Hospital be subject to the same Certificate of Need process as is applicable to non-federal hospitals. It adopted another resolution encouraging the Twin Cities Veterans Administration Hospital to participate voluntarily in the quality assurance and review programs of the local PSRO. That resolution also called for appropriate action to seek amendment of Public Law 92-603 to include all Veterans Administration hospitals under the scope of PSRO quality assurance and review programs.

Though we are skeptical of the cost effectiveness of the Certificate of Need process, so long as community based hospitals are required to participate we feel that the VA Hospital system should be obliged by Congress to operate according to the same rules. For this reason, we have been in contact with our Senators and Representatives urging them to support the recommendations of the Twin City area Metropolitan Health Board for a VA Hospital of reduced bed size. Congressman Sabo should be congratulated for his courage and wisdom in introducing the rider to the Appropriations Bill.

A handwritten signature in dark ink, reading "John K. Meinert M.D." with a stylized flourish at the end.

John K. Meinert, M.D.  
President  
Minnesota Medical Association





**Frederic J. Kottke, M.D., Ph.D.**  
Head of the Department of Physical Medicine and Rehabilitation  
University of Minnesota



# Editorial

## Frederic J. Kottke, M.D.

THOMAS P. ANDERSON, M.D.\*

“WITH GREAT ENERGY and sheer brilliance, Dr. Frederic J. Kottke molded a great Department of Physical Medicine and Rehabilitation at the University of Minnesota. He became the first Director and later Head of the Department. However, Dr. Kottke’s greatest contribution is not the development of his own magnificent department, but the advancement of his specialty in the United States and abroad.” This and hundreds of other testimonials were given by Dr. Kottke’s friends and medical colleagues during the Silver Jubilee Celebration in May, 1978. This celebration marked the twenty-fifth anniversary of the Department of Physical Medicine and Rehabilitation’s establishment. The Jubilee was held, not only to honor the man who has been a department head longer than any person in the Medical School, but to commend Dr. Kottke as a physician, researcher, educator, and humanitarian. He has notably advanced physical medicine and rehabilitation through his tireless efforts and many accomplishments and has earned the respect of his associates by his wisdom, counsel, good-will, and fellowship.

Dr. Kottke has recently announced his decision to step down as Head of the Department of Physical Medicine and Rehabilitation, but will continue his faculty appointment. A search committee to select the Department’s second Head is being organized.

Dr. Kottke was born in Hayfield, Minnesota and grew up in Windom, Minnesota. He earned M.S. and Ph.D. degrees in Physiology, and the Degree of Doctor of Medicine at the University of Minnesota. Dr. Kottke’s contributions to physical medicine and rehabilitation began in the early 1940s when the field was in its infancy and the Department was largely neglected.

Dr. Kottke was completing his formal medical education when the large numbers of disabled military personnel in World War II created a great demand for physicians trained in physical medicine. The gradual realization that disabled individuals who had the opportunity for rehabilitation training could improve the quality of their lives and return to gainful employment prompted public interest in physical medicine. Thus, Bernard Baruch, in memory of his

father, Dr. Simon Baruch, a physician convinced of the efficacy of physical medicine, established an endowment for combined teaching and research programs in physical medicine. In 1945, the University of Minnesota Medical School received a grant for \$40,000 from the Baruch Foundation. Dr. Kottke received training in physical medicine at the University of Minnesota as a Baruch Fellow between 1946 and 1947. He was then appointed Assistant Professor of Physical Medicine and Rehabilitation. In 1949, Dr. Kottke became the Director of the Division of Physical Medicine. At that time the departmental office was housed in a temporary building west of the University Hospitals. During the academic year 1948-1949, the staff of the Division of Physical Medicine was composed of Drs. Knapp, Kottke and Kubicek, 1 clinical instructor, 3 medical fellows, the directors of the schools of physical and occupational therapy, and 3 instructors. One physical therapy supervisor, 4 physical therapists, and one fever therapist treated clinic patients, and research was staffed by two medical technologists.

Under Dr. Kottke’s leadership, the department developed and expanded until, in 1952, Physical Medicine and Rehabilitation was made an autonomous department of the Medical School. By 1954, more room was required and the Department moved to the Seventh and Eighth floors of Mayo Memorial Hospital. As the department continued to provide more comprehensive patient care, teaching, and research programs, still more space was necessary. The six-floor Children’s Rehabilitation Center, housing the inpatient stations, classrooms, and the Schools of Physical and Occupational Therapy, was completed in 1964.

Because of Dr. Kottke’s devotion to the expansion and excellence of the Department of Physical Medicine and Rehabilitation, it now is one of the major providers of rehabilitation care for people in Minnesota and the upper midwest. The present status of the Department’s patient care services, research, and training programs is described in Mildred Olson’s paper, “The Department of Physical Medicine and Rehabilitation in the University of Minnesota Medical School: Patient Care, Education, and Research,” included in this issue. † Dr. Kottke has been concerned, not only with the

\*Professor, University of Minnesota, Department of Physical Medicine and Rehabilitation, Minneapolis, Minnesota.

†See page 557.



development of physical medicine and rehabilitation at the University of Minnesota, but has expended his energies for the welfare of the handicapped at a national level. His efforts have been a major factor in the passage of legislation to benefit the handicapped.

In 1956, Drs. Kottke, Knapp, Krusen, and Ellwood met to discuss the future of the field of Physical Medicine and Rehabilitation. Out of this series of meetings, the concept of Regional Institutes for Medical Rehabilitation was developed. Dr. Kottke's college friend, Senator Hubert H. Humphrey, initiated and supported the necessary bills in Washington, D.C. From 1956 to 1961, Dr. Kottke and the Minnesota physiatrists worked hard documenting the needs of the handicapped population, defining objectives, writing proposals, submitting amendments, and testifying in Washington to obtain the support necessary for the passage of Congressional funds to establish these Centers. Finally, in 1961, their efforts resulted in the appropriation of funds for the first two pilot institutions at New York University and the University of Minnesota. There are now 19 centers; 12 specializing in medical rehabilitation, 3 specializing in vocational rehabilitation, 3 in mental retardation rehabilitation, and 1 in deafness rehabilitation. Annually the Centers conduct over 400 research projects and 900 training projects.

Because of Dr. Kottke's unceasing political efforts, federal funds for rehabilitation rose steadily during the 1950s and 1960s. Other research and training centers were established and, as a result, rehabilitation personnel are being trained in larger numbers, health personnel are gaining increased awareness of the concept of rehabilitation, specialized rehabilitation centers have been established across the nation, research projects are investigating disability and rehabilitation problems, and most important, disabled people are being restored to a fuller and more meaningful life.

At the Silver Jubilee Dinner Program, Dr. Joachim L. Opitz, President of the Minnesota Physiatric Society, presented Dr. Kottke with a certificate from the members. The inscription on this certificate exemplifies the sentiments of Dr. Kottke's colleagues toward his dedication to physical medicine and rehabilitation. "The Members of the Minnesota Physiatric Society as colleagues and beneficiaries of the wisdom, acumen, and teachings of Frederic J. Kottke, M.D., Ph.D. are happy to convey, in this manner, the deep gratitude to him for his tireless energies directed toward the advancement and the enhancement of every endeavor constituted in the manifold discipline of physical medicine and rehabilitation."

### Acknowledgment

The authors of this special issue and Editors of MINNESOTA MEDICINE thank Edna Maneval for her efforts in preparing the manuscripts for submission to the Editors for this special issue.

### New Institutions Accredited for CME

The continuing medical education programs of *St. Olaf Hospital, Austin*, and the *Virginia Regional Medical Center, Virginia*, were recently accredited by the MMA Subcommittee on Accreditation. In addition, the CME programs of *Abbott/Northwestern Hospital, Minneapolis*; *St. Cloud Hospital, St. Cloud*; and *St. Luke's Hospital, Duluth*, were granted reaccreditation. The MMA serves as the accrediting agent of the AMA and of the Liaison Committee on Continuing Medical Education (LCCME) for intrastate providers of CME.



# The Department of Physical Medicine and Rehabilitation in the University of Minnesota Medical School

## Patient Care, Education, and Research

MILDRED E. OLSON, B.S., M.T.\*

The Department of Physical Medicine and Rehabilitation at the University of Minnesota provides patient care, rehabilitation research, and training of physiatrists and other health care professionals. The Rehabilitation Center and several specialty clinics provide both inpatient and outpatient services. Training is provided for physiatrists, occupational and physical therapists, and other rehabilitation professionals. The major categories of research interest are bionomic adaptations, cardiac rehabilitation, ergonomics, neuromuscular, psychosocial-vocational, spinal cord injury, health care delivery, and education in rehabilitation. The departmental staff continually strives to increase the effectiveness of this comprehensive rehabilitation program.

“THE GOAL OF REHABILITATION should be the total societal integration of the individual. A major concern of rehabilitation in medicine is to restore people with continuing handicaps to live as normally as possible in day to day life and provide health maintenance for these people over an entire lifetime.”<sup>1</sup> To these ends, the Department of Physical Medicine and Rehabilitation at the University of Minnesota Hospitals provides

patient care, rehabilitation research, and training of physiatrists and other health care professionals. This paper summarizes the many services, devoted to the rehabilitation of the whole individual, presently available within the Department.

### Patient Care

The University of Minnesota Rehabilitation Center provides a large proportion of the rehabilitation care for the people in Minnesota, as well as of the adjoining states. The director of Rehabilitation Services is Glenn Gullickson, Jr., M.D., Ph.D.

\*University of Minnesota, Department of Physical Medicine and Rehabilitation, Minneapolis, Minnesota.

Supported in part by Grant Number 16-P-56810 (5-17) from the Social and Rehabilitation Service, Department of Health, Education, and Welfare, Washington, D.C., for the University of Minnesota Medical Rehabilitation Research and Training Center.

**TABLE I**  
**Summary of Physical Medicine and Rehabilitation Services**

		1978	
	In- Patient	Out- Patient	Total
Patients Treated	3,373	957	4,330
Patient Visits	42,532	9,667	52,199
Total Treatments	70,456	18,350	88,806
<u>Treatments by Sections:</u>			
Physical Therapy	28,118	14,292	42,410
Occupational Therapy	37,932	2,075	40,007
Speech Therapy	1,916	1,096	3,012
Work Evaluation	1,152	376	1,528
Psychology-Counseling	1,334	511	1,845
<u>Occupational Therapy</u>			
<u>Subtotal by Units</u>			
Rehabilitation Center	13,907	1,333	15,240
Recreational Therapy	2,948	57	3,005
Special Services	21,077	685	21,762



The services of the Rehabilitation Center of the University of Minnesota Hospitals are provided in two areas of the hospital. Patients eighteen years and under receive therapeutic services on the sixth floor of the Children's Rehabilitation Center with the inpatient beds for children located on the fifth floor of this building. The therapeutic services for adults are provided on the seventh floor of the Mayo Memorial Building while the inpatient beds for adults are located on the fourth floor of the Children's Rehabilitation Center.

In 1979, 4,747 patients were seen by the Physical Medicine and Rehabilitation Service. Four thousand three hundred and thirty received treatment from one or more of the therapeutic sections of the Center. Patient visits numbered 52,199 (Table 1). Of the 4,747 patients seen in the rehabilitation services during 1979, a significant proportion were medically indigent. Over 10 percent of the patients seen by the Physical Medicine and Rehabilitation Services were residents from outside of the State of Minnesota. In addition, three occupational therapy programs are provided in the Psychiatric Hospital, the Child and Adolescent Psychiatry Service, and the Masonic Hospital for oncology patients.

Listed in Table 2 are the disease or disability categories for the patients admitted for treatment or services by the Physical Medicine and Rehabilitation Service in 1979. Reflected in the number of patients with mental, psychoneurotic, or personality disorders is the active participation of Occupational Therapy, Work Evaluation, and Counseling Psychology Sections of the Rehabilitation Center with the Psychiatry Service of the University of Minnesota Hospitals. The large number of patients with neoplastic disease

reflects the Occupational Therapy programs in the Masonic Hospital.

The Inpatient Service of the Rehabilitation Center is an integral part of the University Hospitals. During 1979, 392 patients were admitted to the Rehabilitation Center Inpatient Service for an average of 21 days of Rehabilitation Center treatments per patient. Approximately 10 percent of the patients admitted to the Inpatient Service were hemiplegic, 20 percent were paraplegic or quadriplegic, and over 10 percent had cerebral palsy, all major problems for rehabilitation.

The staff is concerned about the disabled person's relationships to family, society, and the community. The teams of professional people in the Comprehensive Rehabilitation Center include occupational therapists, physical therapists, social workers, rehabilitation nurses, work evaluators, speech and language pathologists, clinical psychologists, counseling psychologists, recreational therapists, bioengineers, kinematicians, and medical technologists. The composition of the team depends upon the patient's needs as assessed by the physiatrist, who leads the team and follows the patient's progress through the rehabilitation program. School age children attend the public school, located in the Children's Rehabilitation Center, where teachers with specialized education and training help the children keep up with their school work.

Because the process of rehabilitation requires the close interaction between members of a multidisciplinary team, an understanding of group dynamics is helpful. Dr. Pearl Rosenberg, a social and clinical psychologist, joined the department in 1965. She organized and led a parents' group and a supervisors' group. Dr. Rosenberg is now assistant dean for student

TABLE 2

**Categories of Disease or Disabilities of Patients 1979**

1. Infections and parasite disease	26
2. Neoplasm	203
3. Metabolic disorders, allergies, and nutritional diseases	151
4. Blood dyscrasias	20
5. Mental, psychoneurotic and personality disorders	256
6. Diseases of the nervous system and sense organs	657
7. Diseases of the circulatory system	358
8. Diseases of the respiratory system	12
9. Diseases of the digestive system	14
10. Diseases of the genitourinary system	103
11. Diseases of the skin	33
12. Diseases of the bone and organs of movement	530
13. Congenital malformations	92
14. Symptomatic and ill-defined conditions	1,765
15. Accidents and traumatic injuries	
A. Amputations — 77	
B. Fractures — 184	
C. Sprains, Strains — 90	
D. Lacerations — 86	
E. Burns — 2	
F. Nerve injuries — 24	
16. Speech and Language (not included elsewhere)	64
TOTALS	4,747



affairs in the Medical School of the University of Minnesota.

The Department of Physical Medicine and Rehabilitation offers the services of several specialty clinics: Assessment Clinic, Myelodysplasia Clinic, Pediatric Arthritis Clinic, Muscular Dystrophy Clinic, Hand Clinic, Amputation Clinic, Pediatric Neurology Clinic, Multiple Sclerosis Clinic, and the Pain Clinic. Diagnostic services and research are conducted in the department's laboratories: Neurophysiology Lab, Neuromuscular Disease Lab, Renal Function Lab, Blood Chemistry and Enzymes Lab, Cardiac Function and Energy Cost Lab, Electromyography Lab, Kinesiology Lab, Electronics Lab, and Kinematics Lab.

The staff also cooperates with the other clinical departments in health care programs at the University Hospitals. At the present these include: a Comprehensive Hemophilia Program; a Comprehensive Epilepsy Program; a Pain Treatment Program; an Exercise Program for high risk, absolute bed rest obstetrical patients; a Cardiac Rehabilitation Program for patients on the cardiology service; and a Spinal Cord Injury Program.

The rehabilitation staff also participates in Orthopedic Service Team Rounds and Activities of Daily Living Team Rounds. The Department of Physical Medicine and Rehabilitation provides consultation services to the following departments: Medicine, Surgery, Family Practice, EENT, Ob-Gyn, Pediatrics, Orthopedics, Health Service, Anesthesiology, Neurology/Neurosurgery, Psychiatry, and Urology.

A problem oriented method of charting, first described by Weed<sup>2</sup>, was modified and adapted in 1972 for the special record keeping requirements of the Rehabilitation Center. The problem method of charting has made it easier to follow the progress of patients in the rehabilitation process and has also increased the accuracy and completeness of patients' medical charts. A computer program has been developed to collect data on costs and effectiveness of the rehabilitation process.

### Teaching

The teaching objectives of the faculty of the Department of Physical Medicine and Rehabilitation are to prepare professional rehabilitation personnel to participate in comprehensive rehabilitation and to maintain the competence of those personnel already in the field. During the 1978-1979 University school year, 51 graduate students and 698 undergraduate students were trained by the Department of Physical

Medicine and Rehabilitation. Another 1,186 students participated in continuing education and short courses presented by the Department of Physical Medicine and Rehabilitation and the Sister Kenny Institute under a Federally funded research and training program (RT-2).

The purpose of the Graduate Fellowship Program is to train residents in physical medicine and rehabilitation. This training includes pertinent medical basic sciences with application through clinical practice. The resident's clinical experience is gained through adult and children's inpatient and outpatient services, consultation to all other medical specialties in the University of Minnesota Hospitals, and affiliation with other area hospitals. The residents are encouraged to earn a graduate degree in physical medicine and rehabilitation, either the M.S. or Ph.D. The Department of Physical Medicine and Rehabilitation has trained 182 physiatric fellows since 1948. The present career activities of these graduate residents include academic physiatrists, physiatrists working in government agencies, and physiatrists in private practice. Many heads of physical medicine and rehabilitation departments received their training at the University of Minnesota. There are currently 18 resident physicians in the Department of Physical Medicine and Rehabilitation.

Other graduate courses offered by the Department of Physical Medicine and Rehabilitation are in Physical Therapy, Vocational Counseling, Counseling Psychology, Clinical Psychology, and Speech Therapy.

The major objective of the program "Student as a Physician" is to acquaint the medical student with the nature of the specialty, rather than the techniques, of physical medicine and rehabilitation. The medical students are exposed to the wide range of services carried out by the department, to a great variety of patients, and to the research programs in the department which are related to evaluation and management of disability. Physical Medicine and Rehabilitation provides the medical student with an excellent demonstration of the team approach to total patient care.

The Department of Physical Medicine and Rehabilitation also houses the Schools of Physical Therapy and Occupational Therapy. The Course in Physical Therapy, leading to a bachelor of science degree, trains qualified physical therapists to meet the health care needs of people throughout the nation. Clinical experiences appropriate to the level of training are provided throughout the professional training program



so that skills learned in the laboratory classroom are immediately applied in actual clinical practice. Many affiliated facilities are available for clinical practice. The 1148 Minnesota graduates have outstanding employment placement records.

The Graduate Program in Physical Therapy provides advanced study for qualified, experienced physical therapists. The program has prepared 66 graduates at the Master's degree level for teaching positions in academic programs or in health care facilities providing internships for physical therapy students.

The Course in Occupational Therapy, culminating in a bachelor of science degree, prepares its graduates to work in hospitals and other community facilities. After completing the first two years with a minimal C+ average in biological and behavioral sciences, the student is eligible for admission. Though 114 students applied in 1979, only 30 could be accepted because of limitations of physical facilities and faculty. The program has trained 986 occupational therapists since 1962. Students combine academic work with part-time field work and a minimum of six months on a full time basis in hospitals and community centers throughout the United States. The students in the course have a very low attrition rate, high performance on field work assignments, a remarkable record on the National Certification Examination, and an excellent employment record upon graduation. In addition to the degree program, several continuing education courses and workshops are offered by the occupational therapy faculty.

The Department of Physical Medicine and Rehabilitation also conducts several continuing education and inservice courses in collaboration with Sister Kenny Institute as part of the RT-2 Program. The RT-2 Center is concerned with the maintenance and upgrading of the current level of rehabilitation services by offering short courses which increase the understanding and competence of workers in the allied rehabilitation professions. Refresher courses also have been offered to attract persons who have dropped out of the rehabilitation services and desire to return to work in these professions. Continuing education courses help to diminish the time lag between new knowledge acquisition and application of that knowledge for rehabilitation of the chronically ill and disabled. A number of patient care programs are also taught by the staff.

### Research

Rehabilitation of individuals handicapped by physical, mental, and emotional problems is complex.

Solutions must be found for the problems of the individual, reduction of the disability, acceptance of disability, possibility for compensatory psychophysiological adaptation, career goals, and motivation for rehabilitation. Rehabilitation also includes the patient's relationship in society, family support, community acceptance of the rehabilitation philosophy and adaptability of the community and industry to accept the individual who deviates from the "norm". The professionals in a comprehensive rehabilitation center must deal with all of these problems. In doing so, in each area problems are encountered that can only be resolved in research.

Since the inception of the Regional Rehabilitation Research and Training Center in 1962, 251 research projects have been completed. At present there are 22 continuing research projects, 5 new studies, and 8 proposed research projects. Many of these are long range research projects directed toward the solution of difficult problems, for example, prevention of ischemic ulcers and urinary tract infections. Research is, however, designed to spread broadly across the needs of rehabilitation medicine to study problems which cause continuing disability. The major categories of research interest in the Department of Physical Medicine and Rehabilitation are: bionomic adaptations, cardiac rehabilitation, ergonomics, neuromuscular, psychosocial-vocational, spinal cord injury, health care delivery, and education in rehabilitation.

The research projects on bionomic adaptations have investigated the value of equipment routinely used in rehabilitation centers, making recommendations for any needed changes, and investigated the design of particular orthoses. Specialized equipment has been created. A series of studies on ergonomics has dealt with muscular strength in disabled persons. Mr. Martin Mundale is in charge of a Kinesiology Laboratory equipped with instrumentation appropriate for assessing strength and work of muscles.

Though various aspects of cardiac disease have been considered, many of the research projects have dealt with the use of the Minnesota Impedance Cardiograph developed by William Kubicek, Ph.D. and bioengineers, Robert Patterson, Ph.D. and David Witsoe. The Minnesota Impedance Cardiograph has been incorporated into a system that simultaneously records: (1) the impedance wave form, which indicates the heart's pumping action; (2) heart sounds; and (3) the electrocardiogram.

The impedance system has been used to study the cardiac function of normal control subjects, as well as patients. Cardiac work requirements of hospital and



rehabilitation activities are studied by continuous recording of oxygen consumption, heart rate, electrocardiogram, respiratory ventilation, and intermittent estimation of cardiac work. Base-line studies of cardiac function and systolic time intervals are done by the Department of Physical Medicine and Rehabilitation on cardiac patients, including patients with coronary artery disease; patients who have artificial pacemakers; patients with aortic, mitral, and/or other heart valve problems; and patients recovering from myocardial infarctions. The Impedance Cardiograph has been clinically tested throughout the world, and is now being used in acute coronary care centers to monitor patients with myocardial infarctions, in surgical recovery rooms to follow patients after cardiac surgery, and in work evaluation laboratories to evaluate cardiac performance during test activities.

Over 80 research studies have been conducted by the researchers in the Department of Physical Medicine and Rehabilitation dealing with causes of neuromuscular disease and treatment and retraining of the patients. In the neuromuscular physiology laboratory, directed by Dr. Daniel Halpern, a training program for upper extremity activities in the athetoid patient has been evolving over the years. The program is based upon some current concepts about the relationship between posture and voluntary motor activity. Specialized equipment has been designed to test and record the progress of athetoid patients toward controlled use of their hands and arms. The computer is used extensively in these studies.

Neuromuscular diseases are studied in the electromyography laboratory directed by Dr. Essam Awad. Muscular abnormalities have been studied by light microscopy, electron microscopy, and enzyme chemistry of blood and muscle. Basic research in the ultrastructure of cells and nerves through the use of the electron microscope is also being conducted. Dr. Rita Bistevins' Ph.D. thesis was on the study of the Golgi tendon organ in human muscles and tendons.

Other neuromuscular research projects have been conducted to investigate the problems of: contractures of connective tissue, impaired communication and speech in the physically disabled population, paranatal central nervous system damage, brain damage in adults, communication deficits, and auditory evoked potentials.

The staff has conducted over 52 studies on psychosocial problems in rehabilitation. More recent projects include biofeedback research and followup studies of patients in the Pain Treatment Program by Dr. Alan Roberts; a followup study of the psychological, social, and vocational adjustment of spinal cord

injured adults by Dr. Gary Athelstan; a functional assessment inventory for rehabilitation evaluation by Dr. Nancy Crewe; and the results of "mainstreaming" disabled children into a regular classroom situation by Dr. Jessie Easton. Other psychosocial projects have investigated topics such as the vocational placement of disabled individuals, motivational studies, and attitudinal studies.

One of the emphases of research in the RT-2 Center has been the study of patients suffering from spinal cord injuries. A series of studies on the effect of pressure on the production of decubital ulcers has demonstrated a correlation between prolonged local external pressure exceeding capillary pressure and ulcer formation. Work on the problem of ischemic ulcers was started in 1957 by Dr. Michael Kosiak who measured pressure under the ischial tuberosities and 10 other points of normal subjects.<sup>3</sup> Reliable methods for relieving sitting pressure at short intervals for wheelchair patients are still under investigation. Work is continuing toward the improvement of the pressure testing system through the utilization of solid state sensors. Also continuing is the development of a chair seat that will relieve pressures under people who cannot move themselves.

Another long-term spinal cord injury research project is on the study of urologic function in patients following spinal cord injury. In 1962, Dr. Mary Price began a study of renal function of paraplegic and quadriplegic patients. Now in its 17th year, the project has a population of approximately 500 patients with spinal cord injury who return annually for a complete evaluation of their renal function and re-evaluation of their general status. Findings demonstrated that with good care, renal function does not deteriorate. The personnel in the Renal Function Laboratory have developed techniques for obtaining uncontaminated urine specimens, studied the sources of urinary tract infection in patients with ileac diversions, implemented patient education programs in urinary tract care and urinary collection devices, and published manuals on urinary tract care for both health care professionals and patients.<sup>4,5</sup>

Other studies on spinal cord injured patients have included investigations of job possibilities, communication problems, emission of sperm, and alterations in cardiovascular control. Based on the research in this area and quality of patient care, in 1974, a Spinal Cord Injury Center was established at the University of Minnesota. Dr. Keith Sperling, Medical Director of the Spinal Cord Injury Center, leads a team of physicians in Physical Medicine and Rehabilitation, Orthopedic Surgery, Neurosurgery, and Urologic



Surgery. This team directs the entire care spectrum relating to spinal cord injury and extends efforts to the prehospital phase via the Emergency Medical Services as well as to the Metropolitan Health Board for health care planning.

In response to the demands of the government and third party payers, the staff of the Department of Physical Medicine and Rehabilitation has conducted a number of projects dealing with health care delivery. Projects such as "Studies of Rehabilitation Outcomes" and "Evaluation of Outcome of Rehabilitation Measured by Costs of Rehabilitation and Maintenance and Changes in Quality of Life" have provided health care professionals with data on the ability of patients to maintain their levels of achievement once they have left the Rehabilitation Center. A number of other health care delivery projects have dealt with the development of efficient data storage and retrieval and cost accountability in rehabilitation.

Rehabilitation medicine has faced the problem of developing an educational process which can compete favorably with crisis medicine. Physicians in practice have had inadequate exposure to the process for rehabilitation management in medicine and most medical faculties have been conditioned to pay little attention to this aspect of medicine. Several research projects have dealt with this problem. The last research project completed regarding education in rehabilitation concluded that the degree of exposure to rehabilitation medicine during medical school is positively associated with later effective practice behavior in dealing with chronically ill and severely disabled individuals.

### Support Staff

The teaching, research, and patient service staffs have access to a variety of educational materials and to people who can assist in the preparation of audiovisual aids and research papers. These people include the library staff, a media resource person who produces 16

mm films and does video taping, an editor, and a medical illustrator.

The specialty library of the Department of Physical Medicine and Rehabilitation contains almost 4,000 books, about 16,000 slides, 100 cassette tapes and 75 eight mm films, and receives about 100 journals. In December, 1977, this library was formally designated THE MILAND E. KNAPP LIBRARY, honoring Dr. Knapp for his more than 50 years of continuous teaching and services to Physical Medicine and Rehabilitation at the University and his pioneering work in establishing physical medicine as a recognized specialty in the field of medicine.

The total staff of the Department of Physical Medicine and Rehabilitation now includes over 300 people. The Department has completed its growth and developmental phase and is well into productive maturity in all areas. Continued growth will be dependent upon the continued recognition by the federal government that the problems of disabled people have not all been solved and that financial support of research and teaching at the RT centers will need to continue.

### Conclusion

Through the effort of the Physical Medicine and Rehabilitation departmental staff, care is provided to a wide variety of patients of all ages who have physical disabilities and psychological problems. The staff is strongly committed to advancing rehabilitation services through applied research studies, thus increasing the knowledge of disabling and chronic diseases. An equally strong commitment exists toward training enough health care professionals to serve the needs of the state and the region. The departmental staff continues to recognize the social, economic, and psychological factors influencing the relationship between the handicapped or disadvantaged person and society, thus increasing the effectiveness of the comprehensive rehabilitation program.

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# Myotonometry

## A Quantitative Technique to Measure Muscular Hypertonia

DANIEL HALPERN, M.D.;\* ROBERT BECK, B.E.E.† and DEBRA NESSE, B.A.‡

**Myotonometry evaluates muscle tone quantitatively and yields reproducible data that can be permanently recorded. This method of evaluation is based on measurements of the force applied and angular position of a joint subjected to passive motion. The angular movement of the body part is recorded by a potentiometer. By using statistical analysis, the slopes, or dynamic indices, and the intercepts on the ordinates, or static indices, of each of the regression lines may be tabulated so that the characteristics of response may be inspected and further analyzed. The elements contributing to spastic and dystonic characteristics of muscle tone in hypertonic patients may be identified and distinguished from one another. This method of analysis provides a useful tool for assessing treatment of hypertonia.**

**T**HE CLINICAL CARE of patients with muscular hypertonia would be more effective if a quantitative method for measuring muscle tone was available. The objective evaluation of medications, surgery, intramuscular or peripheral neurolysis, or motor training procedures all require quantitative, reproducible data that can be permanently recorded. The comparison of the status of individuals with spasticity or dystonia under different conditions and at different times has always been a difficult task. Clinical evaluation has often been unreliable, especially when the proprioceptive memory of the examiner is the basis for the judgment. A quantitative method of evaluating hypertonia to measure the strength of involuntary reflex patterns observed in patients with central nervous system disorders also is needed. The value of treatment can be assessed and the information may be helpful in interpreting neurophysiologic events in the intact patient. In addition, a reproducible quantitative measurement of muscle tone would be useful if the data were in terms that coincided with current views of neuromotor organization.

This study presents myotonometry, a method of evaluation of muscle tone that fulfills the previously mentioned requirements.

Muscle tone is determined to a large extent by the influence of the fusimotor system on the anterior horn cells in the spinal cord<sup>1</sup>, together with other systems of the central nervous system, acting directly or indirectly on the anterior horn cell<sup>2</sup>. The fusimotor system, as described by numerous neurophysiologic studies<sup>3</sup>, causes muscle, through its innervation by the anterior horn cell, to respond to two aspects of an imposed change in length. Where inhibition from higher centers is diminished, as in the decorticate, decerebrate, or spinal cord injured individual, the muscle will respond to the parameters of change in length, as well as velocity of change. The responsiveness of the fusimotor system to each of these parameters differs in terms of frequency, amplitude, duration, and characteristics of inhibition or facilitation by diverse influences. The response to velocity of motion is the primary characteristic of the myotatic reflex as elicited by deep tendon reflex or clonus. In spastic individuals this response is called dynamic activity. The response to elongation is exemplified by the resistance to passive motion in spastic or dystonic individuals and is referred to as static activity. Similarly, anterior horn cell firing may be influenced from spinal or supraspinal loci in response to visual or contactual stimuli, or to joint, body, or head position without the intervention of the fusimotor system. Many of these characteristics may be identified clinically by passively moving the patient's limbs while varying the stimuli under study. Without quantitative determinations, however,

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changes in the status of these interactions are difficult to document.

The creation of a system of recording and analyzing the responsiveness of muscle contraction to joint movement thus enabling analysis of these factors was proposed. A principle measuring the force required to move a limb passively through its range of motion at various speeds has been used in previous studies of hypertonia. Methods of data analysis in these studies are varied.

Webster<sup>4</sup> has shown that a quantitative evaluation of the total amount of work done in the course of the movement may be calculated from the area enclosed by two curves representing a plot of torque acting through a range of passive motion as measured by angular excursion. Using this procedure, however, it is not possible to analyze the data for information describing the relevant physiological parameters. Poppele and Terzuolo<sup>5</sup> have described a system of analysis of the myotatic reflex in which input-output relations are expressed in terms of gain and phase as a function of frequency. This procedure examines the properties of the myotatic reflex but does not describe them in terms that are easily related to clinical observation. Herman<sup>3</sup> and his colleagues have developed a technique of evaluation of spasticity that involves passive motion of an ankle at varying speeds with a recording of the changes in tension during the cycle of motion. This method is useful, but still limited in the convenience of quantitation of the various physiologic effects that should be observed.

### Method

Myotonometry is based on measurements of the force applied and angular position of a joint subjected to passive motion. The angular movement of the body part is recorded by a potentiometer. The potentiometer and a hydraulically powered rotor are attached to the limb under study. The external force required to influence the imposed movement of the limb is recorded by a load cell interposed between the rotational device and the limb (Figure 1). The limb may be moved manually or by hydraulic power according to any special requirements of the patient. The signals generated by these transducers are amplified and conditioned, and are then fed to a Midwest light beam oscillograph, and simultaneously to a Terak digital computer. Electromyographic recordings are made of the direct, rectified, and averaged action potentials of the opposing groups of muscles. Torque values can be computed from the forces recorded by the load cell.

A limb is passively moved through a maximum range of motion in both directions. Each such movement constitutes a single cycle. A series of 36 cycles is carried out in random order, at speeds varying approximately from 3°/second to 150°/second. Usually four cycles are run for each of nine speeds. The patient relaxes between cycles. The angular velocity is controlled as the limb is moved by hand by visually observing the movement of a spot of light, governed by the potentiometer output<sup>6</sup>, on a cathode ray oscilloscope. A duplicate spot of light on the oscilloscope is caused to move at a predetermined speed, and the operator attempts to keep the two dots superimposed or moving parallel to one another. When hydraulic power is used, a feedback control system maintains constant velocity at any selected value.

From these data the angular values during the course of the movement in both directions together with the simultaneously applied forces are recorded.

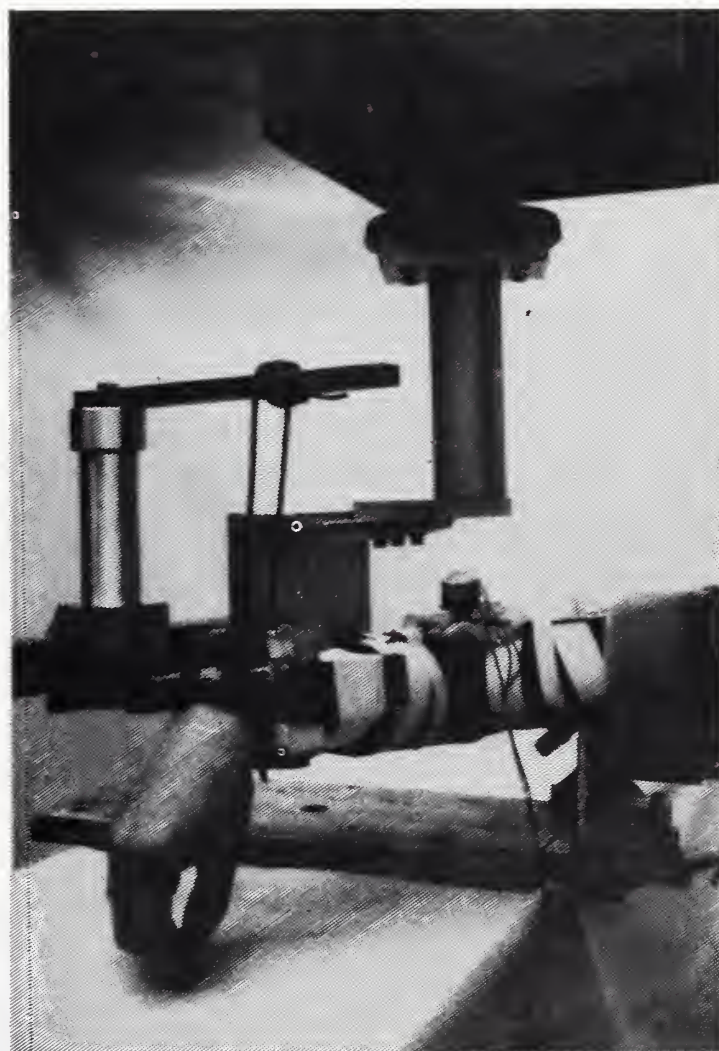


Fig. 1 — Shows the upper limb in the hydraulic rotatory apparatus arranged to record muscle tone of biceps and triceps muscle groups. The potentiometer above the elbow records angular position, and the load cell proximal to the wrist monitors the force applied during motion.



# LAKE MINNETONKA EXECUTIVE COUNTRY ESTATES



Historically set on Upper Lake Minnetonka's Smithtown Bay, Boulder Bridge Farm, originally known as Rose Farm, was settled by Edmund J. Longyear in the mid 1800's. Considered one of the most beautiful country estates in Minnesota, Rose Farm entertained many a distinguished guest.

In 1920 the estate was acquired by George Draper Dayton who promptly changed the name to Boulder Bridge Farm in light of the architecturally marvelled boulder foot bridge enhancing the entrance to the estate's private lagoon from Smithtown Bay.

Nationally noted for his development of livestock breeding, as well as business success in establishing Dayton's Drygoods, George Draper Dayton's Boulder Bridge Farm was heralded worldwide. Boulder Bridge's fame grew steadily with its herd of Guernsey cattle producing 4 National Champion cows, 218 championships and 598 first prizes at state and national exhibitions and over 400 A.R. records.

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### Dynamic Index

A statistical approach is used to isolate the element of velocity-responsiveness of the muscle spindles. As the passive movement is imposed upon a joint, the force applied simultaneously with the angular change of position is recorded. In each cycle of movement a point in time corresponding to a predetermined constant angle is selected. At this constant angle in both phases of each cycle (Figure 2) the instantaneous force being applied and the simultaneous velocity are read and plotted against one another. When these points are recorded a scattergram is obtained from which a regression curve may be calculated (Figure 3). The steepness of the slope of the regression line indicates the velocity-responsiveness of the system and, therefore, a quantitative measure or index of the myotatic or dynamic response. The dynamic index, or slope of the regression line, may be expressed in terms of Newton-centimeters/degree/second to conform to standard scientific nomenclature. One Newton is equivalent to 0.225 pounds force, and 1 Newton-centimeter is equivalent to .0089 inch-pounds.

### Static Index

The responsiveness to length, or static index, of the

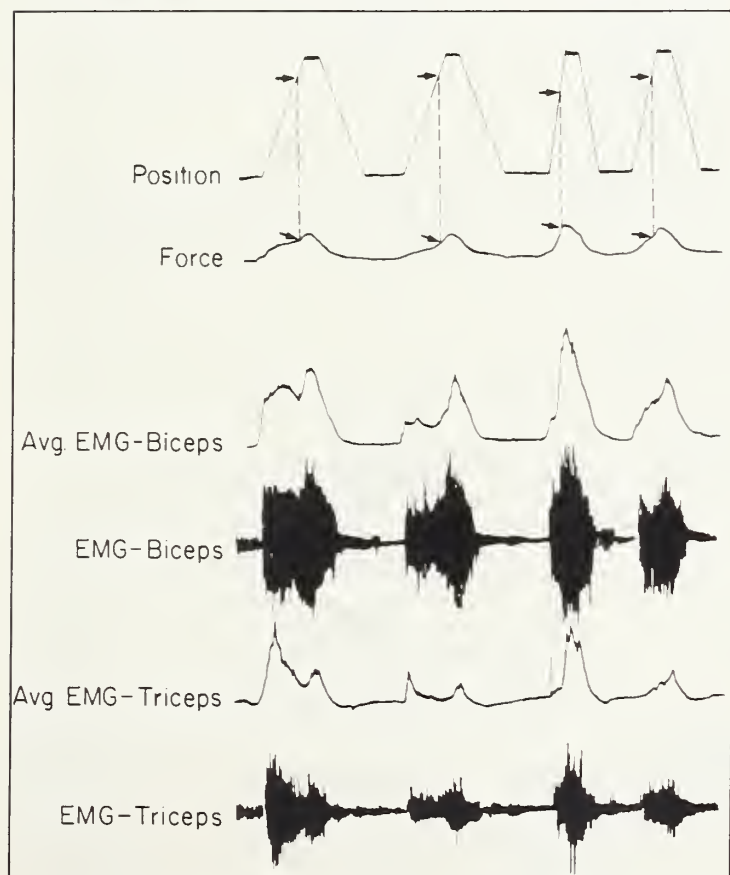


Fig. 2 — Simultaneous display of angular position, force applied, and electromyographic activity during a series of motion cycles. The arrows on the position display indicate an arbitrarily selected angle at which the velocity is measured. The dotted lines indicate the moment in time at which the force applied to the limb is read.

### TORQUE VS. VELOCITY AT 73.3 DEGREES

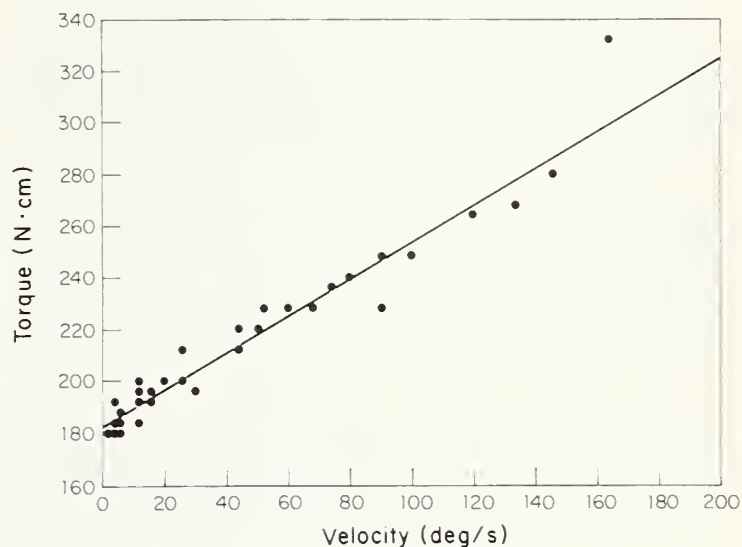


Fig. 3 — Scattergram and regression line calculated for a single angle in each of 36 cycles of passive motion. The torque is plotted on the ordinate and velocity along the abscissa.

muscle group being observed may be derived (Figure 3) by noting the torque indicated as the intercept of the regression line on the ordinate, or y-axis. This value is a function of the muscle activity at the angle chosen for observation extrapolated to hypothetical zero velocity. In this manner, the influence of length on the muscle tone can be separated from that of velocity and independently measured, since the torque at zero velocity is a function of the angle of limb position.

By selecting several angles distributed across the range of motion, scattergrams and regression lines may be plotted for each position of the limb. An assessment of the behavior of the neuromuscular response to stretch may now be carried out over the entire range of motion of the limb. A family of regression lines at these selected angles may then be displayed graphically. The slopes, or dynamic indices, and the intercepts on the ordinates, or static indices, of each of the regression lines may be tabulated so that the characteristics of response may be inspected and further analyzed (Table 1).

The data in Table 1 were obtained for a patient with spasticity and moderately severe dystonia. The static index, and the dynamic index of the flexor and the extensor muscles of the elbow were identified for a series of angles evenly distributed through the range of motion. The angles selected were arbitrarily chosen to be 12.5%, 27.5%, 42.5%, 57.5%, 72.5%, and 87.5% of the maximum range of motion of the joint whose controlling muscles were being examined. These angles give a good representation of the motor



responsiveness at equal intervals through the range of motion. They eliminate the initial and terminal 12.5% of motion during which plastic or structural resistances to passive motion or other irrelevant phenomena might be encountered. The Table includes standard deviations for each of the computed indices, as well as a correlation or Rho value, which is a measure of the relative dependence upon velocity exhibited by dynamic index. Thus, while the absolute value of the dynamic index is an indication of the sensitivity of the fusimotor system to velocity, the correlation, Rho, is a

measure of its dependence on velocity as compared with other influences which may be operative during the experimental or examination procedure.

These data may be reduced by averaging the static and dynamic indices, identifying the maximum values and calculating the rates of change of static and dynamic activity with change in length of the muscle. Table 2 illustrates this process as applied to the information in Table 1. In this way, a single numerical value can represent a specific activity corresponding to a specific functional aspect of the muscle spindle

**TABLE 1**  
**Static and Dynamic Indices at Constant Angles**

Axis: Left Elbow

Diagnosis: Cerebral palsy — Spastic quadriplegia

Range of Motion: 60-150°

Position: Seated, head midline

Angle Degree	Extension		Correlation Rho
	Static N-m	Dynamic N-cm/deg/s	
71.3	1.23 ± .29*	1.39 ± .37*	.54
84.6	1.99 ± .26	2.49 ± .27	.84
98.3	3.12 ± .33	2.56 ± .30	.83
111.8	4.19 ± .31	2.93 ± .30	.86
125.3	5.23 ± .27	2.98 ± .29	.87
138.8	6.40 ± .24	4.36 ± .40	.88

Angle Degree	Flexion		Correlation Rho
	Static N-m	Dynamic N-cm/deg/s	
71.3	-0.63 ± .22*	2.68 ± .35*	.80
84.6	-0.40 ± .24	1.26 ± .32	.56
98.3	-0.61 ± .18	.85 ± .23	.54
111.8	-0.84 ± .12	.50 ± .13	.54
125.3	-1.51 ± .17	.42 ± .19	.36
138.8	-3.12 ± .18	.22 ± .23	.16

\*Standard error

**TABLE 2**

Axis: Left Elbow

Diagnosis: Cerebral palsy — Spastic quadriplegia

Range of Motion: 60-150°

Position: Seated, head midline

	Static Activity	
	Biceps	Triceps
Mean Static Activity (N-m)	3.69	-1.18
Maximum Static Activity (N-m)	6.40	-0.40
Elongation Response (N-m/deg)	.078	.034
Biceps-Triceps Equilibrium (degrees)	—	61.0

	Dynamic Activity	
	Biceps	Triceps
Mean Dynamic Activity (N-cm/deg/sec)	2.79	.99
Maximum Dynamic Activity (N-cm/deg/sec)	4.36	2.68
Angle Maximum Dynamic Activity (degrees)	139.0	71.0
Dynamic-Elongation Interaction (N-cm/deg <sup>2</sup> /sec)	.035	.032



system. The data were graphically displayed in order to examine the responsiveness to stretch through a range of motion. Plots of the slopes of the torque versus velocity, the dynamic indices, against a series of limb angles were made (Figure 4(A)). Similar graphs of the static indices, plotted against the limb angles were also made (Figure 4(B)).

The observations in this paper are based on ninety-eight patients who had been examined a total of 299 times by myotonometry. Although any muscle may be measured using this method, this paper will relate findings in the elbow flexors, primarily the biceps brachii. The individual results reported are representative of findings in the various clinical conditions.

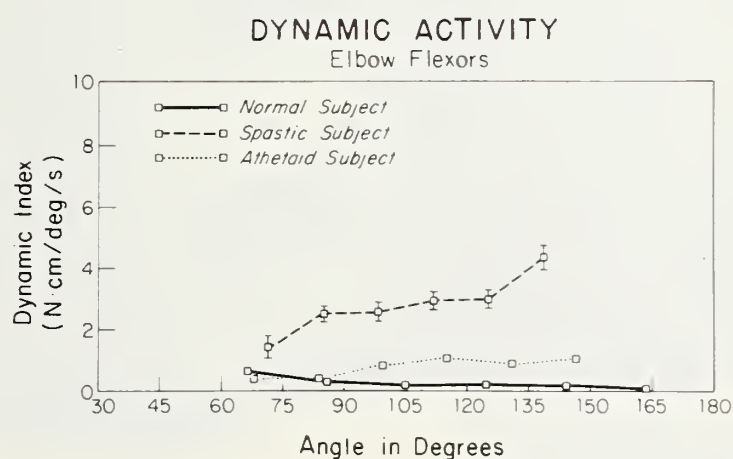


Fig. 4(A) — The dynamic indices (slopes) at each of six selected angles in the range of motion are displayed for a normal subject, an athetoid and a spastic patient.

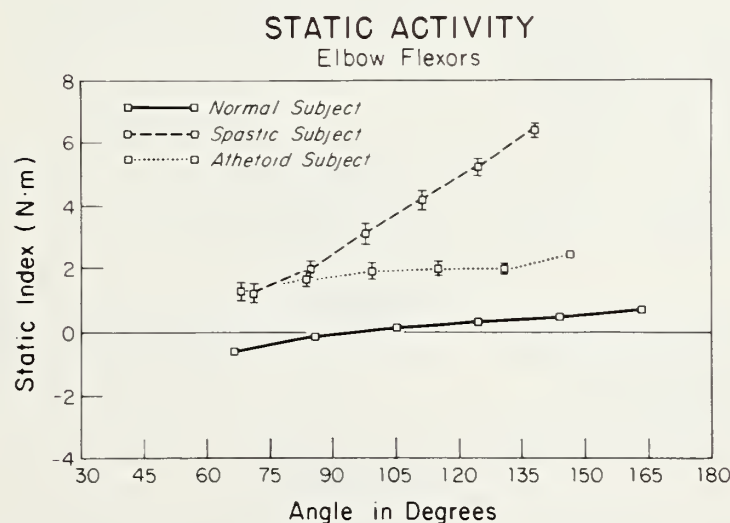


Fig. 4(B) — The static indices (ordinate intercepts) at each of the six selected angles in the range of motion are displayed for a normal subject, an athetoid and a spastic patient.

## Results

### Dynamic Activity

The static and dynamic indices for the elbow flexors behave in a characteristic manner in different patients, and under different circumstances, in accord with their clinical status.

A Mean Dynamic Index, indicating the general magnitude of dynamic activity, was determined by averaging the values of the dynamic indices measured at each angle chosen, in the range of motion tested. The maximum dynamic index was noted in the course of the stretch and the angle at which this occurs. A maximum dynamic index significantly above the average dynamic index would suggest a strong myotatic reflex, or clonus occurring at that angle of stretch.

### Dynamic-Elongation Interaction

A consistent rise in the level of dynamic activity with angular change or muscle stretch would imply a facilitatory effect on dynamic action associated with stretch. The usual values of length-dynamic interaction seen clinically in normal individuals are at the general level of .001 to .002 Newton-centimeters/degree<sup>2</sup>/second. Normative data are still being collected, and, therefore, statistically reliable values are not available at this time.

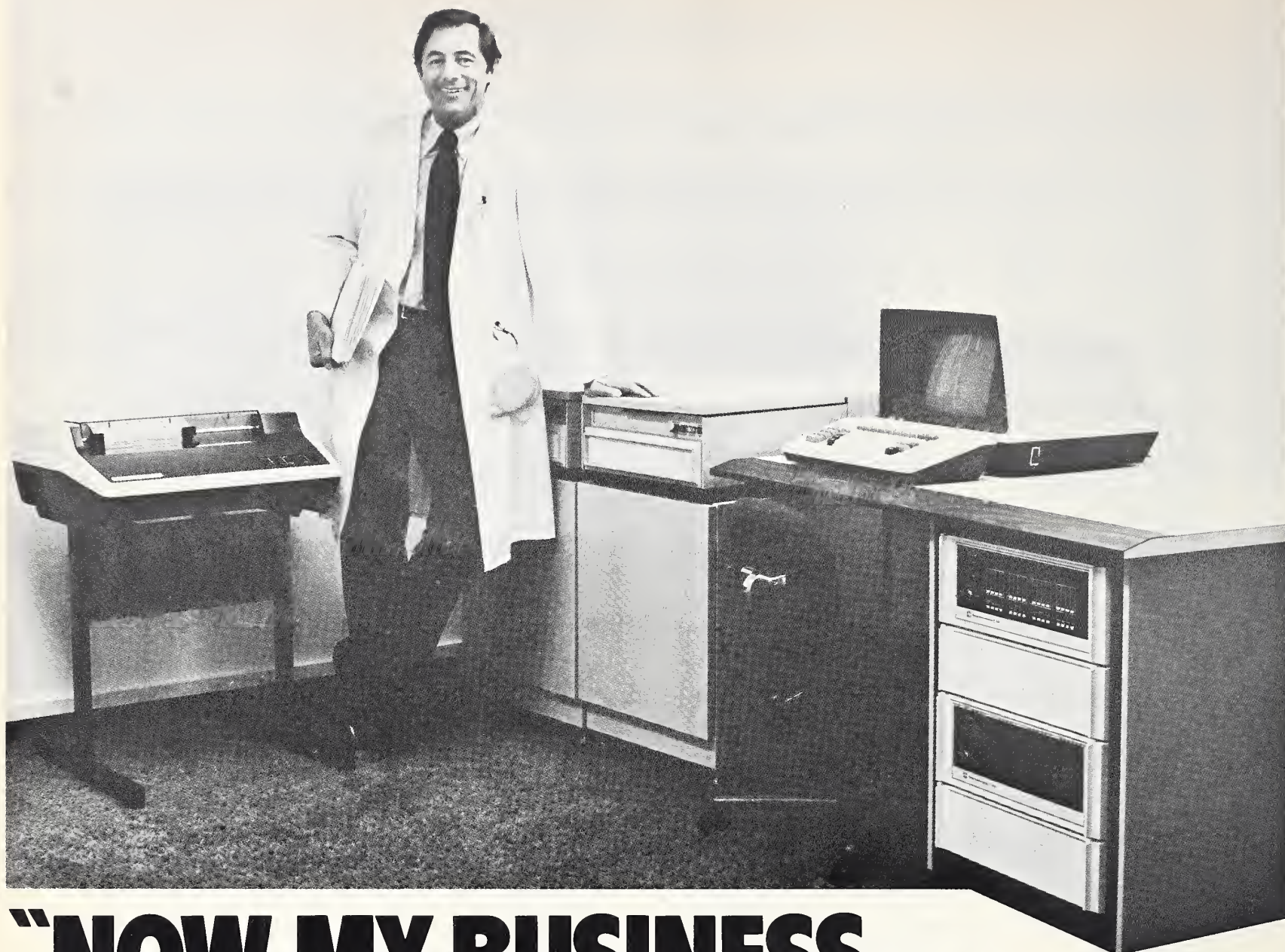
### Static Activity

If a graph were made of the intercepts on the ordinate of the family of regression curves plotting them against the angles at which they were determined, a visual representation would be obtained of the alteration of static responsiveness with muscle length (Figure 4(B)). An average of the static indices determined for the six selected angles establishes a numerical value for the Mean Static Activity throughout the range under the conditions tested. In the biceps, normal individuals show a low value (less than 1.0 Newton-meter or .074 foot-pounds) of Mean Static Activity.

### Elongation Response

A graphic display of the static indices through the range of motion tested is usually fairly flat, or shows a slope in the biceps brachii of less than .05 Newton-meter/degree in normal individuals (Figure 4(B)). As a result of this gradual inclination an objective definition of equilibrium of the opposing muscle activities acting on the elbow can be made from examination of the behavior of the static index of the biceps and the triceps muscles. The angle at which the agonist-antagonist muscle groups exert equal static activity would represent the angle of equilibrium in





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muscle tone, and, therefore, would indicate the preferred posture.

### Clinical

The normal subject and the athetoid patient show low velocity responsiveness or dynamic activity. The values typically observed were below 1.0 Newton-centimeter/degree/second in individuals without spasticity. Furthermore, the correlation value,  $Rho$ , for the spastic patient approached 0.8. In patients in whom poor volitional control existed, the correlation value,  $Rho$ , was sometimes even higher. Normal individuals who have inadvertent muscle activity and athetoid patients with no clinical evidence of spasticity show a poor relationship to velocity responsiveness. There are some exceptions to this rule.

The static activity may be used to study the activity of supraspinal reflexes as shown in Figure 5. In a similar manner, other spinal and supraspinal reflexes or the effects of medication (Table 3, Figure 6) may be measured quantitatively.

### Discussion

Myotonometry quantitatively and objectively measures muscle reactions to the stimulation of stretch. The information obtained is closely related to the behavior of the muscle spindle and its control systems, as presently conceived. The influences of head position and limb posture may be quantitatively evaluated by this system as well. The dynamic and static activity of a selected muscle group may be characterized by a single numerical value for any

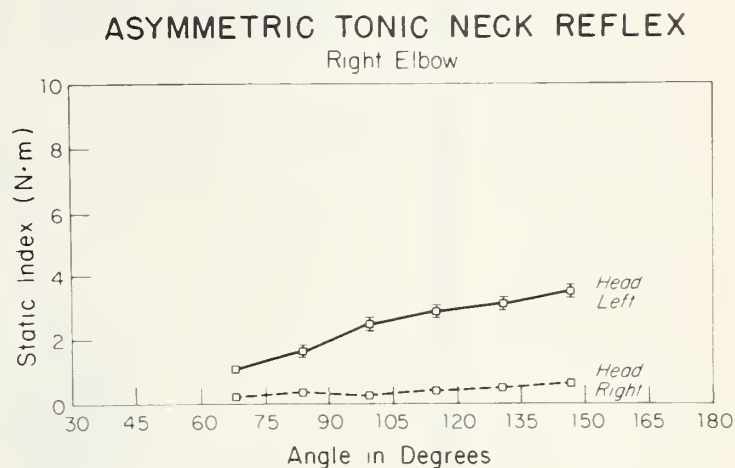


Fig. 5 — The strength of the asymmetric tonic neck reflex may be evaluated by measuring the static activity of the biceps with the head turned to right and left.

specific joint angle or as a mean value over the range of motion measured. The numerical values are in relevant physical terms, which would be expressed as Newton-meters for static activity, and Newton-centimeters/degree/second for dynamic activity. The interaction, if any, between the two parameters of spindle activity may also be observed graphically or numerically. The relative activity of antagonistic muscles surrounding a joint can be compared and the distribution of postural tone defined objectively.

The static activity, as defined, is held to correspond to the concept in which this reflex activity is associated with the intrafusal nuclear chain muscle fiber, secondary afferent nerve fiber system<sup>7</sup>. The dynamic

TABLE 3

Axis: Left Elbow  
Diagnosis: Cerebral palsy  
Range of Motion: 45-125°  
Position: Lying on right side.

	Static Activity — Biceps	
	without medication	with medication
Mean Static Activity (N·m)	1.63	.64
Maximum Static Activity (N·m)	3.49	1.06
Elongation Response (N·m/deg)	.059	.013
	Dynamic Activity — Biceps	
	without medication	with medication
Mean Dynamic Activity (N·cm/deg/sec)	2.90	1.06
Maximum Dynamic Activity (N·cm/deg/sec)	5.45	2.27
Angle Maximum Dynamic Activity (degrees)	116.0	116.0
Dynamic-Elongation Interaction (N·cm/deg <sup>2</sup> /sec)	.087	.039



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activity is interpreted to correspond to the model usually assigned to the nuclear bag intrafusal muscle fiber and Ia afferent nerve fiber system. The static activity describes the response of the system to changes in length of the muscle, and dynamic activity describes the response of the system to velocity. The observation in Figures 4(A) and 4(B), that spastic patients show an elevated level of static and dynamic activity is in accord with clinical observations. Athetoid patients, similarly, show elevated levels of static activity, but dynamic activity is within normal limits as long as spasticity is not also present.

The data also demonstrate that spastic patients show a clear enhancement of both the dynamic and static activity with elongation of the muscle. Thus, while the dynamic activity, the dynamic-elongation interaction, and the static elongation responses all reflect some aspect of the fusimotor system activity level, the mean static activity level represents dystonia of any origin, including the fusimotor system.

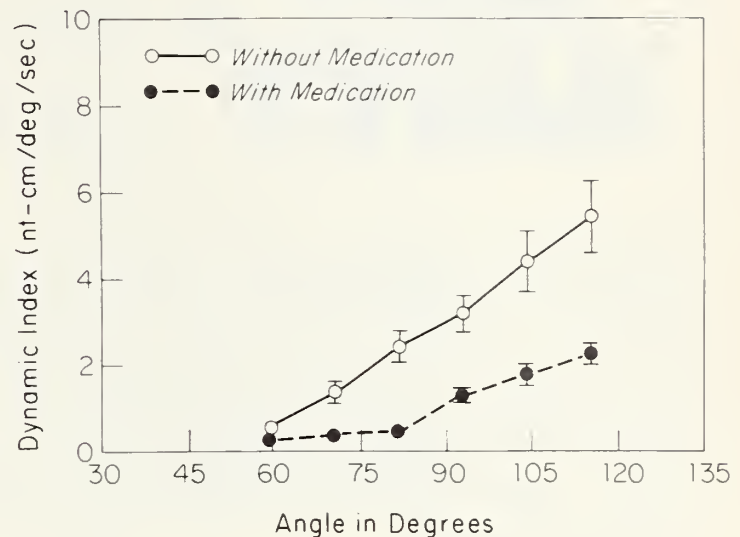
Two important factors contributing to the resistance to passive stretch of muscles are viscous and elastic elements of the musculotendinous structures. Viscosity provides a resistance proportional to velocity of motion, and elasticity provides resistance proportional to the extent of elongation. These factors appear to be low in the elbow flexors and extensors.

Muscles differing in anatomical structure, as well as bulk, may, therefore, be expected to show different levels of static and dynamic activity on structural and neurophysiologic bases. Normative data will be necessary for appropriate interpretation.

Myotonometry, as presented here, is essentially a clinical procedure and depends for its interpretation on concepts derived from basic neurophysiologic information.

The advantage of myotonometry is that the static and dynamic activity and their interactions with muscle elongation are measured quantitatively to evaluate overall function of the fusimotor system in particular and central nervous system control of muscle tone in general. Analysis of the clinical condition of the patient, or the results of a treatment can be effectively pursued with a noninvasive technique. The response of the central nervous system to training programs, postural maneuvers, medications, or surgical procedures may be quantitatively observed (Figures 6(A) and 6(B)). An objective clinical guide relating to the adequacy or effectiveness of treatment is, therefore, available.

### Dynamic Activity



### Static Activity

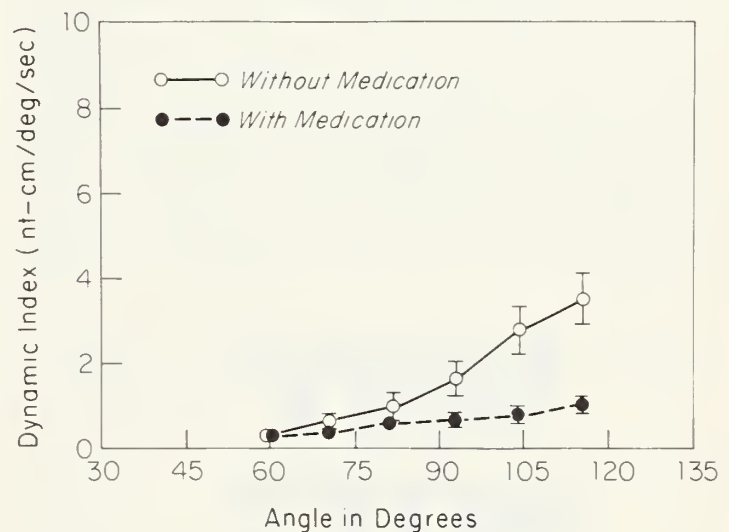


Fig. 6 — The effect of a medication on spasticity may be measured by observing the dynamic activity (A-top) and the static activity (B-bottom) of the biceps during myotonometry.

### Conclusion

Neuromuscular activity in the hypertonic patient may be quantitatively measured. The elements contributing to spastic and dystonic characteristics of muscle tone may be identified and distinguished from one another. The specific parameters of spindle responsiveness, the dynamic activity of the muscle spindles corresponding to the reaction to the rate of lengthening, and the static activity corresponding to the reaction to length, may each be numerically defined. The interaction between the two spindle system components, as well as the change of static activity with length itself, may also be specifically identified and quantitated. This method of analysis provides a useful tool for assessing treatment of hypertonia.



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Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** **Cardiovascular:** Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Central Nervous System:** Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. **Gastrointestinal:** Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. **Allergic:** Urticaria, rash, ecchymosis, erythema. **Endocrine:** Impotence, changes in libido, gynecomastia, menstrual upset. **Hematopoietic System:** Bone marrow depression, agranulocytosis, leukopenia. **Miscellaneous:** A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

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References: 1. Citations available on request from Medical Research Department, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon [Dillon], R.H., and Leyland, H.M.: A comprehensive review of diethylpropion hydrochloride. In, Central Mechanisms of Anorectic Drugs, S. Garattini and R. Samanin, Ed., New York, Raven Press, 1978, pp. 391-404.

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# Use of Oxygen Uptake Measurements in Cardiac Stress Testing

ROBERT P. PATTERSON Ph.D.\* and WILLIAM D. REMOLE, M.D.†

This study of 52 patients undergoing a progressive exercise stress test added continuously measured  $O_2$  uptake to the other parameters normally measured. If the  $O_2$  uptake is divided by the pulse rate, a parameter called  $O_2$  pulse results. By using the Fick equation, this parameter can be equated to the product of the stroke volume times the A- $VO_2$  difference. The direct measurement of the  $O_2$ /beat/kg parameter during a cardiac stress test gives information about the efficiency of the circulatory system and of the possible mechanisms involved in the performance improvement.

THE PROGRESSIVE exercise stress test is widely used in clinical cardiology to manage and evaluate patients with coronary artery disease. Although it has wide use, many studies<sup>1-3</sup> have shown significant false negatives in male patients. Recently, Fortuin and Weiss<sup>4</sup> reviewed nine studies that correlated the stress test results based on the EKG with the results of angiography in symptomatic patients. The results showed a sensitivity (true positives/true positives + false negatives) of approximately 65%.

Other information besides the positive or negative results based on the EKG can be obtained from the stress test. For example, the patient's blood pressure response or work level at the conclusion of the test can be determined. From this information, estimates can be made about the level at which the patient can safely work, although many physicians feel unsure about the accuracy of these estimates.

The purpose of the present study was to add continuously measured  $O_2$  uptake to the other parameters measured during the stress test. From these parameters, the actual aerobic portion of the work can be measured and a better estimate of the ability of a patient to work at various levels can be made. If the  $O_2$  uptake is divided by the pulse rate a parameter called  $O_2$  pulse results. By using the Fick equation, this parameter can be equated to the product of the stroke volume times the A- $VO_2$  difference. An increase in this parameter reflects an increase in the efficiency of the cardiovascular system. If the A- $VO_2$  difference

increases for a given work activity due to the greater extraction by the peripheral tissues, the oxygen delivery to the tissue will increase without any increase in myocardial work. Many recent studies<sup>5,6</sup> have shown that myocardial oxygen consumption, which measures the input energy to the heart, correlates very well with heart rate. For a given cardiac output, a reduction in heart rate and an increase in

Measured METs vs. predicted METs during a treadmill stress test on normals.

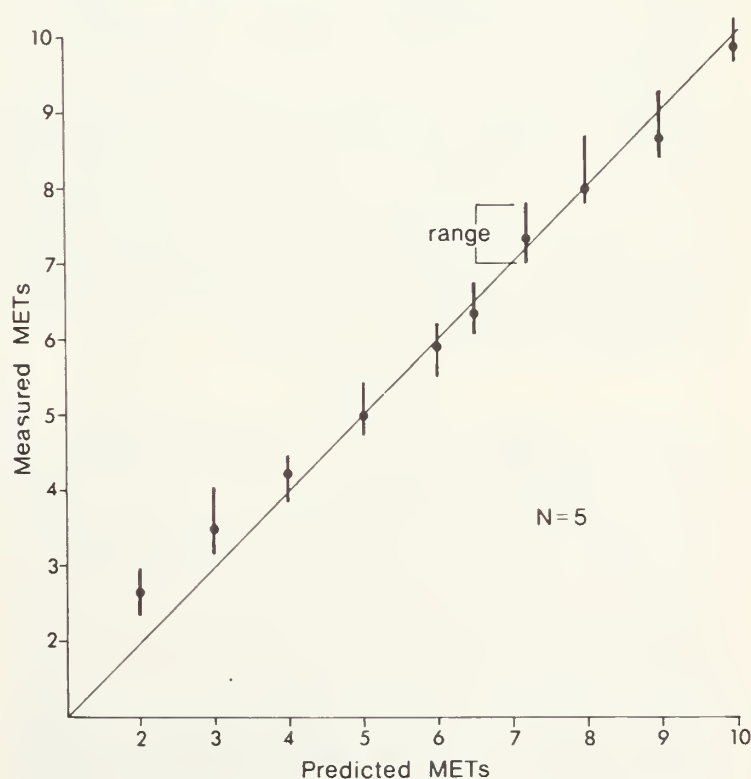


Fig. 1 — Comparison of the measured and predicted MET level of 5 normal subjects undergoing a progressive exercise stress test on the treadmill. The vertical bars represent the total range of the data.

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stroke volume will result in a reduction in myocardial work. This result occurs with physical conditioning and also with beta adrenergic blocking drugs such as propranolol which suppresses heart rate. Therefore, an increase in either of these parameters with exercise at a given work load reflects an increase in the efficiency of the circulatory system. Bruce *et al.*<sup>7</sup> has reported that one of the most significant physiological parameters that reflects a decrease in cardiac function in patients with coronary artery disease is the stroke volume, whereas the parameter that shows the most improvement with physical conditioning in patients with cardiac diseases is the A-VO<sub>2</sub> difference.

### Methods

The study was conducted on 52 patients undergoing a progressive exercise stress test using a modified Naughton protocol.<sup>8</sup> The work load was increased 1 MET (1 MET = resting oxygen consumption or 3.5 ml O<sub>2</sub>/kg) every 2 minutes. An extra step was added between the 6 and 8 MET levels which results in the steps being 6, 6.5, 7.2, and 8 METs. This was done to reduce the rate of increase at a point where many patients typically stop. The oxygen consumption was measured using a quadruple mass spectrometer system developed in the laboratory along with a Thermal-Systems Inc. hot film flowmeter. Electronic circuitry was developed that computes the oxygen uptake on a breath-by-breath basis for recording and displays the O<sub>2</sub> uptake updated each minute. A standard 12 lead electrocardiogram was recorded using a Marquette recording system. Ten patient tests were repeated after approximately one year in the course of normal patient management. The predicted MET level for a given grade and speed of the treadmill was based on the values reported by Naughton.<sup>8</sup> Five normal subjects (22-35 years) were also evaluated to observe the trend in parameters for normals.

### Results

Figure 1 shows the results plotting the measured METs versus the predicted METs for five normal subjects. The results of plotting the same parameters in 52 patients is shown in Figure 2. The vertical bars indicate the range of the data with the short cross bar indicating the standard deviation. Figure 3 shows a plot of the O<sub>2</sub>/beat/kg of body weight versus the difference between measured METs minus predicted METs for a normal subject. The small numbers next to the data points indicate the MET level of the work. As an O<sub>2</sub> deficit occurs, which would be indicated by a significant fall in the measured MET level below the

Measured METs vs. predicted METs during treadmill stress test performed on patients.

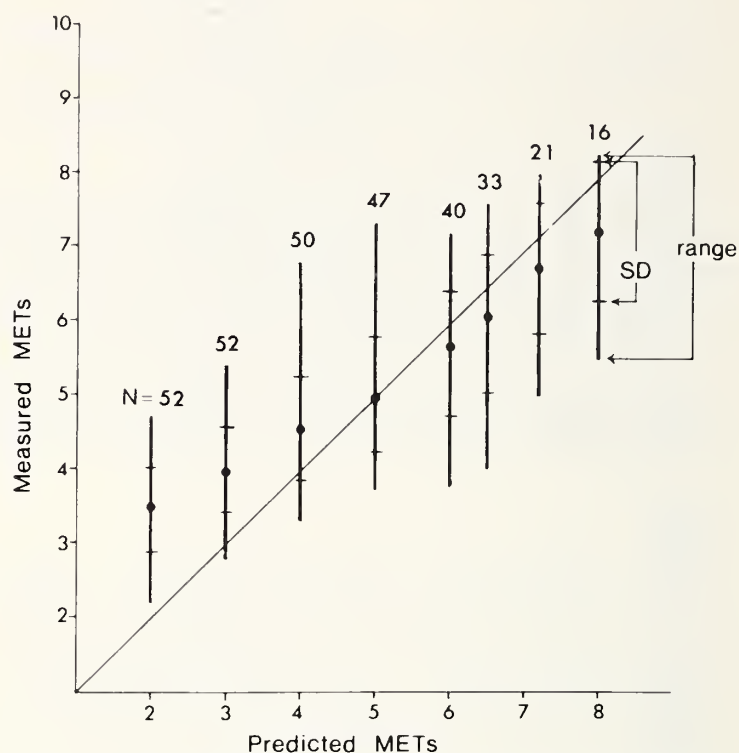


Fig. 2 — Comparison of the measured and predicted MET level of 52 patients undergoing a progressive exercise stress test on the treadmill. The vertical bars represent the range of the data with the cross bars showing one standard deviation.

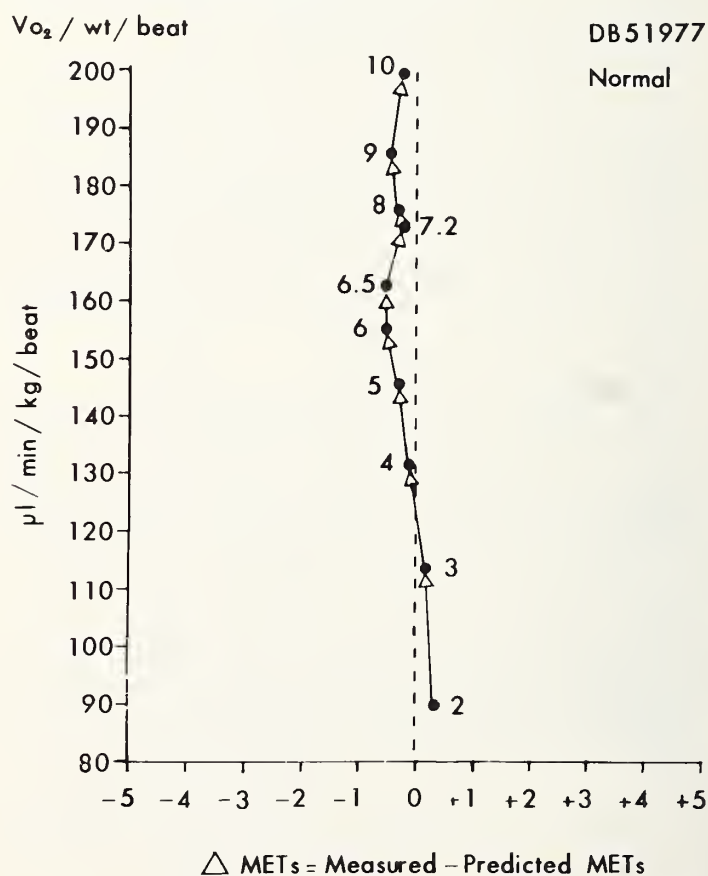


Fig. 3 — The O<sub>2</sub> uptake/beat/kg of body weight versus the difference between the measured and predicted MET level for a normal subject undergoing an exercise stress test. The small numbers next to the data points represent the predicted MET level of the exercise.



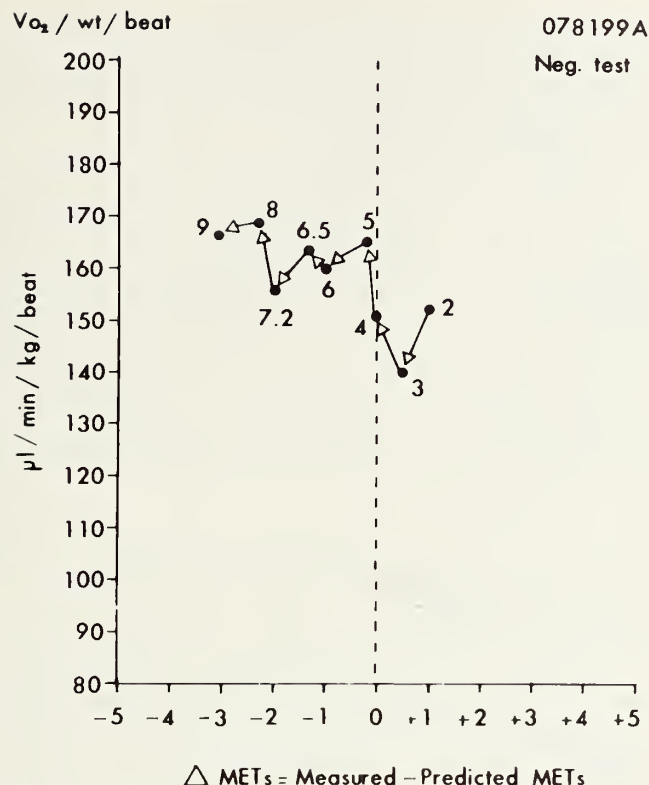


Fig. 4 — The  $\text{O}_2$  uptake/beat/kg of body weight versus the difference between the measured and predicted MET level for a patient in whom the coronary arteries were bypassed. The small numbers next to the data points represent the predicted MET level of the exercise. This is an example of a patient in whom an  $\text{O}_2$  deficit develops.

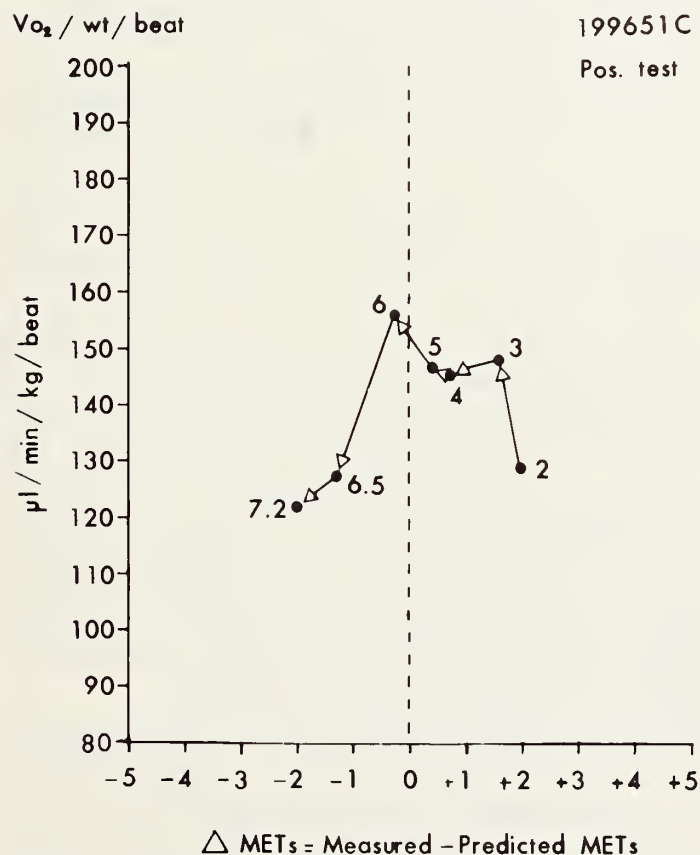


Fig. 5 — The  $\text{O}_2$  uptake/beat/kg of body weight versus the difference between the measured and predicted MET level for a patient with significant coronary artery disease. The small numbers next to the data points represent the predicted MET level of the exercise. This is an example of a patient in whom the stroke volume most likely showed a significant fall after the 6 MET level.

predicted value, the graph will move to the left. Figure 4 shows the results from a patient who had coronary artery bypass surgery. This patient shows little increase in the  $\text{O}_2/\text{beat}/\text{kg}$  and also an apparent large  $\text{O}_2$  deficit occurs. Figure 5 shows a patient with coronary artery disease in which the  $\text{O}_2/\text{beat}/\text{kg}$  falls after the patient passes the 6 MET level.

A patient with 80% stenosis of the left circumflex coronary artery and 90% stenosis of the left anterior descending artery is shown in Figure 6 before and after a regular exercise program was started. Figure 7 shows the improvement of the  $\text{O}_2/\text{beat}/\text{kg}$  parameter after coronary artery bypass surgery. Before the surgery, the  $\text{O}_2/\text{beat}/\text{kg}$  decreased after the 3 MET level while after the surgery the parameter increases up to the 7.2 MET level.

### Discussion

The results comparing measured versus predicted METs in patients show relatively large variation compared to the normal subjects who were familiar with treadmill walking. At the low MET levels at the start of the test it is commonly observed that patients have a very unnatural or awkward gait which becomes

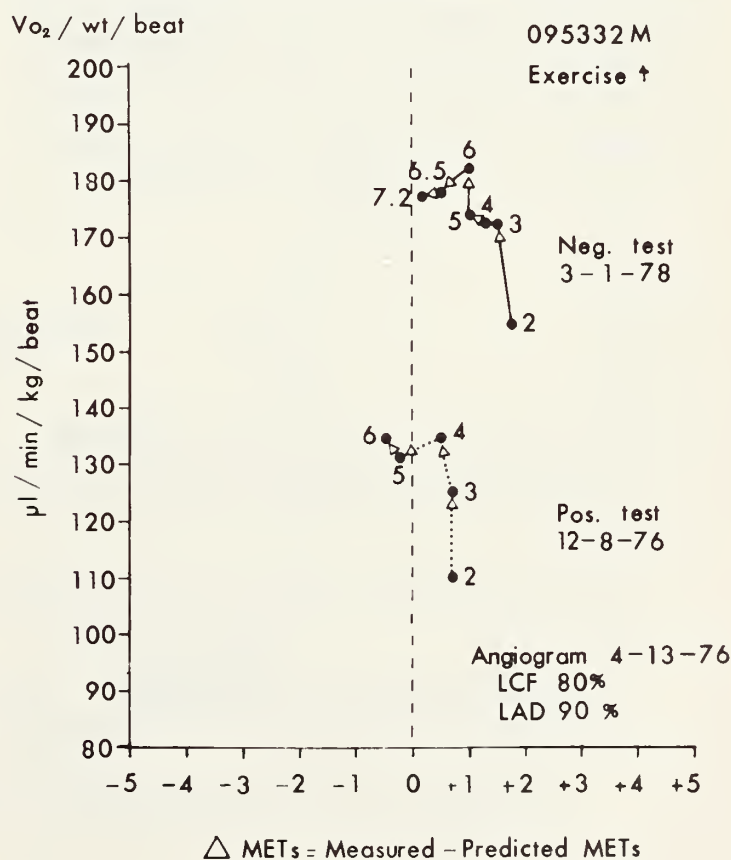


Fig. 6 — The  $\text{O}_2$  uptake/beat/kg of body weight versus the difference between the measured and predicted MET level for a patient with significant coronary disease. The small numbers next to the data points represent the predicted MET level of the exercise. The data shows the results before and after a patient started on the exercise program. The angiogram results show the percent stenosis of the left circumflex (LCF) coronary artery and the left anterior descending (LAD) coronary artery.



more natural after coaching and with time on the treadmill. This causes the mean measured METs to exceed the predicted value. With some patients, it was observed that at 3 or 4 minutes the  $O_2$  uptake falls due to the change to a more natural gait. At the higher work levels, the mean measured MET level falls below what would be predicted presumably due to the development of oxygen deficit.

The relatively large variation in the measured MET level of work for a given speed and grade setting of the treadmill suggests that accurate predictions of aerobic work capabilities cannot be made on the basis of time on the treadmill or the MET level reached. This is supported by the studies of Froelicher et al.<sup>9,10</sup> in which they also found large individual variations in the maximal  $O_2$  uptake when correlated with time on the treadmill. This is in conflict with reports by Bruce et al.<sup>11,12</sup> in which they suggest that the maximal oxygen uptake and an individual's functional aerobic impairment can be determined from the time on the treadmill, age, and activity status. Bruce et al. tend to develop their work based on means and correlative relationships, whereas Froelicher concentrates more on the

variability of the data. Because of the nature of the disease, it seems more appropriate to be concerned about the cardiac patient whose test results fall at the outer ranges of the data.

In Figure 3 the  $O_2$  uptake per beat parameter shows an approximately 100% change for a 10 MET work load in a normal subject with little deviation of the measured MET level from the predicted MET level. In Figure 4 the results for a patient with bypassed coronary arteries show only a 13% change in the  $O_2$  uptake/beat/kg and also an oxygen deficit over an equivalent of 3 METs. Figure 5 shows a case in which the  $O_2$ /beat/kg begins to rise at the start of the test, but at the 6 MET level the parameter begins to fall along with the development of apparent  $O_2$  uptake equivalent deficit of 2 METs.

Bruce et al.<sup>12</sup> and Hanson et al.<sup>13</sup> have shown that the A- $VO_2$  difference increases in a linear manner with the work load. Therefore, a fall in the  $O_2$ /beat/kg strongly suggests a fall in the stroke volume. The extraction of oxygen by the peripheral tissues should not fall, resulting in a decrease in the A- $VO_2$  difference as the work load increases. From the data given by Bruce et al.<sup>11</sup> a 9 MET work load should result in at least a 50% increase in the A- $VO_2$  difference. Therefore, the small increase in the  $O_2$ /beat shown in Figure 4 would indicate a fall in the stroke volume as the work load increases.

The increase in the  $O_2$ /beat/kg occurring after an exercise program as shown in Figure 6 is most likely a result of an increase in the A- $VO_2$  difference resulting from peripheral conditioning and an increase in the stroke volume concurrent with bradycardia resulting from training. Hanson et al.<sup>14</sup> showed that both stroke volume and A- $VO_2$  difference increased with training in normal middle aged men whereas Detry<sup>15</sup> showed that only A- $VO_2$  difference showed a statistically significant increase with training in patients with coronary artery disease. The increase in the  $O_2$ /beat/kg seen in Figure 7 as a result of coronary artery bypass surgery is most likely due to stroke volume improvements because of the improved perfusion of the heart although after surgery some patients more faithfully adhere to a suggested exercise program.

In the past, the increase of maximal oxygen uptake due to conditioning has been attributed to an enlargement of the maximal oxygen delivery by the central circulation caused mainly by a cardiac stroke volume improvement. Recent literature suggests that physical conditioning results in both an increase in stroke volume and a larger A- $VO_2$  difference at submaximal work loads.<sup>13,14,16</sup> In the middle-aged,

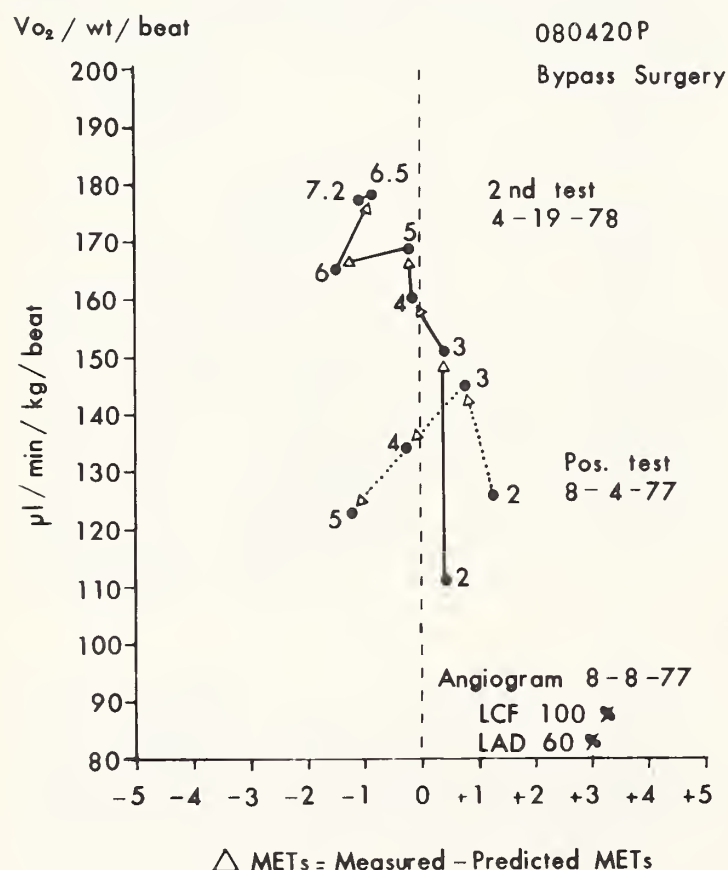


Fig. 7 — The  $O_2$  uptake/beat/kg of body weight versus the difference between the measured and predicted MET level for a patient in whom the coronary arteries were bypassed. The data shows both before and after results. The small numbers next to the data points represent the predicted MET level of the exercise. The angiogram data refers to the percent stenosis of the left circumflex (LCF) coronary artery and left anterior descending (LAD) coronary artery before surgery.



healthy individual a significant stroke volume increase<sup>14,17</sup> occurs with conditioning whereas for the patient with coronary artery disease, the improvement in A-VO<sub>2</sub> difference is the principal factor<sup>13,16,18</sup> in work performance improvement. In this study, some patients with coronary artery disease have a larger increase in the O<sub>2</sub>/beat occurring than could be explained by assuming only an A-VO<sub>2</sub> difference improvement. The increase in the overall level of the O<sub>2</sub>/beat/kg due to conditioning of the cardiac patient, as seen in Figure 6, is most likely caused by an increase in A-VO<sub>2</sub> difference with stroke volume increase a

significant factor only for some patients. The shape of the response pattern in a given test is most like the result of the stroke volume response.

The direct measurement of the O<sub>2</sub>/beat/kg parameter during a cardiac stress test gives information about the efficiency of the circulatory system and of the possible mechanisms involved in the performance improvement. Both the magnitude of the O<sub>2</sub>/beat/kg and the pattern of change during a progressive test add significantly to the cardiovascular evaluation obtained with a progressive exercise stress test.

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#### Cover Photograph “Life”

Dr. Carl M. Kjellstrand, Professor of Medicine and Surgery and Chief of the Division of Nephrology at the University of Minnesota, took the cover picture in Sequoia National Park in California in 1973.

The Editors feel that “Life” is an appropriate name for this lovely scene for it is obvious in this beautiful setting that the little tree’s hold on in organic matter is only a very temporary one.

This is not the first time that the covers of MINNESOTA MEDICINE have been graced with one of Dr. Kjellstrand’s snapshots. His March, 1979, cover “Early Spring in Minnesota” won the outstanding award for best cover for that year.

Dr. Carl Kjellstrand came to the United States in 1962 from Sweden. He is a graduate of the University of Lund in Sweden.



# Quality of Life

## The Ultimate Goal in Rehabilitation

NANCY M. CREWE, Ph.D.\*

**Quality-of-life studies and their pertinence to rehabilitation medicine are discussed. A University of Minnesota study defined a wide range of long-term outcome measures as part of a followup study of spinal cord injured persons. In general, the patterns of the variables in this investigation do not conform to the traditional versions of adjustment. The findings of John Flanagan and several other rehabilitation researchers are reviewed. The results of quality-of-life studies will further document the cost-effectiveness and impact of rehabilitation medicine in improving the quality of life for disabled persons.**

**Q**UALITY OF LIFE is an idea that is being discussed currently in several contexts, including medicine. Americans are asking that physicians go beyond their traditional goal of adding years to life and concern themselves with the issue of how to make those added years worthwhile. Improving quality of life is not a new idea in the field of rehabilitation medicine, but additional work is needed to develop explicit and observable outcome measures. Until this is done, recognition and tangible support will continue to focus exclusively on the economically justifiable goals of physical restoration and vocational rehabilitation. Improvements in quality of life will be acknowledged only in so far as they are by-products of more "legitimate", that is, measurable, outcomes.

This paper will describe a study, conducted at the University of Minnesota, that sought to identify some broad criteria of long-term adjustment among people with spinal cord injury. It will also review quality of life measures developed by several other researchers in medicine and psychology. Finally, it will propose the application of techniques generated in a general nationwide study to assess the quality of life among disabled Americans.

The Minnesota study defined a wide range of long-term outcome measures as part of a followup study of spinal cord injured persons. The adjustment of spinal cord injured persons in a large number of life areas was evaluated. Data were organized and an operational definition of overall adjustment or of quality of life after disability was developed.

Subjects first were surveyed by means of mailed questionnaires. Then intensive interviews were conducted with 128 spinal cord injured people and 66 of their significant others (usually a parent or spouse). The questionnaire covered a detailed description of their current life situations and ratings of satisfaction with various areas of their lives. The interview concerned their lives since the time of injury. Information was obtained about their health and medical treatment, educational and work experiences, social life, sexual and marital adjustment, and their feelings about their disability and about themselves. A spouse or parent was also questioned about the impact of the injury on the individual and the family.

Data were collected on 33 variables that were judged to reflect different aspects of "adjustment". To determine the relationship among these variables, the data were analyzed in two steps. First, a matrix was generated in which each of the variables was correlated with every other one. This resulted in a total of 528 correlations ranging from  $-.32$  to  $+.89$ . The vast majority were positive and 60% were statistically significant.

Next, a cluster analysis was done and the results of this procedure are shown in the Figure. (See next page.)

The results are too complex to be presented in detail. There are indeed clusters, but they are not divided neatly along content lines. Some separation occurs between how the individual views his own adjustment, which tends to cluster on the left side, and the way that others view it, which is mostly on the right side.

Several variables were almost separate. For example, employment and the use of free time seem to be

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little related to the other variables. The same can be said for the ratings of medical adjustment. This suggests that on the whole people who work are not necessarily healthier, less disabled, or better off psychologically than those who do not work. In general, the patterns of variables do not conform very well to the traditional or armchair versions of what constitutes adjustment.

Several other rehabilitation researchers have also published papers on rehabilitation outcomes and/or quality of life. Stanley Smits<sup>1</sup> conducted a comprehensive study in which he defined rehabilitation success using 10 Likert scaled items: employment status, physical functioning, self care, activities outside the home, self-consciousness, knowledge about conditions, social relationships, participation in family, independent outlook, and affective outlook. He

summed the scores on the 10 scales to arrive at a numerical index of success.

Roberta Trieschmann<sup>2</sup> defined the goal of rehabilitation as teaching each disabled person to cope with disability at the functional level of which the individual is capable. Three criteria of coping were specified: (1) prevention of medical complications and utilization of ADL and mobility skills; (2) maintenance of a stable living environment; and (3) productivity.

"The Quality of Survival of the Cancer Patient" by A. B. Cobb<sup>3</sup> listed the five following factors as essential to a quality survival: (1) health quality, particularly whether the individual is bedfast or up and about; (2) comfort, defined as freedom from pain or the distress of limited activity; (3) functions, including ability to manage activities of daily living and work; (4) emotional response, how well the individual has

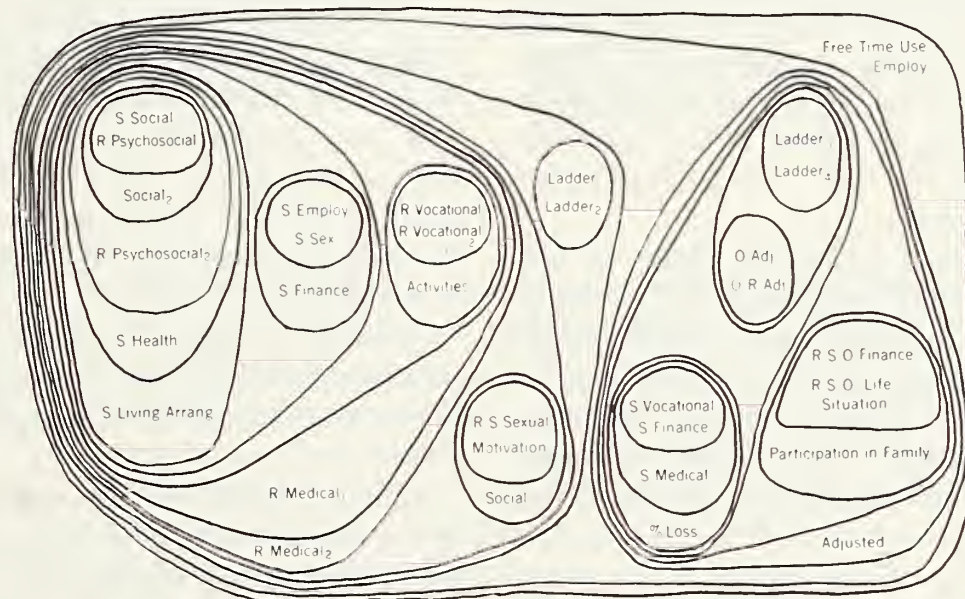


Figure  
(Variables listed by cluster from left to right)

S Social: Self rating of satisfaction with social activity  
R Psychosocial1: Counselor rating of psychosocial adjustment, based on mailed questionnaire  
Social2: Extent of current social activity  
R Psychosocial2: Interviewer rating of psychosocial adjustment  
S Health: Self rating of satisfaction with general health  
S Living Arrang: Self rating of satisfaction with living arrangements  
S Employ: Self rating of satisfaction with employment  
S Sex: Self rating of satisfaction with sex life  
S Finance: Self rating of satisfaction with financial situation  
R Medical1: Counselor rating of medical adjustment based on mailed questionnaire data  
R Medical2: Interviewer rating of medical adjustment  
R Vocational1: Counselor rating of vocational adjustment based on mailed questionnaire  
R Vocational2: Interviewer rating of vocational adjustment  
Activities: Total score on activities index  
Ladder 1: Self rating of adjustment (1-10), present time  
Ladder 2: Self rating of adjustment (1-10), expectations for future  
R S Sexual: Interviewer's rating of satisfaction with sex life  
Motivation: Interviewer's rating of motivation for independence  
Social 1: Extent of social activity shortly after spinal cord injury  
S Vocational: Interviewer's rating of satisfaction with vocational

situation  
S Finance: Interviewer's rating of satisfaction with financial situation  
S Medical: Interviewer's rating of satisfaction with medical situation  
% loss: Self rating of loss due to injury  
Ladder 3: Rating by family member of spinal cord injured person's adjustment (1-10), present time  
Ladder 4: Rating by family member of spinal cord injured person's adjustment (1-10), expectations for future  
O Adj: Rating by family member of own adjustment (1-10), present time  
O R Adj: Rating by family member of own adjustment (1-10), expectations for future  
Free time use: Involvement in leisure activities  
Employ: Involvement after spinal cord injury in paid work  
R S O Finance: Interviewer's rating of the family member's satisfaction with financial situation  
R S O Life situation: Interviewer's rating of the family member's satisfaction with life situation  
Participation in family: Interviewer's rating of spinal cord injured person's participation in family  
Adjusted: Self rating of overall adjustment



accepted himself or herself and adjusted back into the family and community; and (5) economics.

Levy and Wynbrandt<sup>4</sup> published a paper entitled, "The Quality of Life on Maintenance Haemodialysis." They identified the following variables as measures of quality of life: (1) income (most patients suffered a severe loss in income); (2) sexual activity (most patients reported a diminished sex life); and (3) life style (rated on the basis of the degree to which patients had resumed their major life activities).

An editorial in the *Journal of The American Medical Association* was published in 1976 on quality of life by Samuel Vaisrub<sup>5</sup>. His view is less complex, though not unique in the history of rehabilitation. He seems to equate quality of life with employability, stating that for unemployed persons, "the attained quality of life is apt to be void of social usefulness".

Three main goals of rehabilitation were identified by Peter Wax<sup>6</sup>: achievement, interaction, and inner resources. He wrote that rehabilitation programs should encourage and teach patients to develop a rich inner life which would increase autonomy and make being alone less painful.

The papers that have addressed quality of life outside of a medical or rehabilitation framework would be too numerous to mention, however, one major research effort directed toward improving the quality of life of Americans deserves special attention. Conducted by psychologist John Flanagan<sup>7</sup>, it may provide the basis for significant new work in rehabilitation.

Flanagan began by defining quality of life in an empirical manner. His group collected 6,500 critical incidents from nearly 3,000 people of varying ages, races, and backgrounds representing all areas of the country from Harlem to retirement communities in Arizona to San Francisco's Chinatown. Subjects were asked questions like, "Think of the last time you did something very important to you or had an experience that was especially satisfying to you. What did you do or what happened that seemed so satisfying and why?" Other questions focused on things that were harmful or made life worse, the biggest change in quality of life during the past five years, a continuing source of trouble, a strong positive impact, and a strong negative impact. The 6,500 incidents were sorted into categories involving similar types of behavior and experiences. With gradual refinement, 15 quality-of-life categories were formulated.

The next phase of the study involved interviews with a nationally representative sample of people to assess the quality of life for adults and the most promising

opportunities for improving it. Flanagan and his associates conducted three-hour interviews with 1,000-30 year olds, 600-50 year olds, and 600-70 year olds. Each of the latter samples is being brought up to 1,000, but was not complete at the time of the recently published report.

To briefly summarize Flanagan's findings, most adults report that their needs and wants are well met in the areas most important to their quality of life. About 85% of the 50 and 70 year olds reported their overall quality of life to be good, very good, or excellent. Another major finding was the striking similarity between the responses of people in the three age groups and of the men as compared with the women.

Although Flanagan's questions were not identical to the satisfaction questions asked in this followup study, an interesting comparison of the responses is possible. In the Minnesota study, subjects were asked "How satisfied are you with the following aspects of your life?" They responded on a five-point scale ranging from very satisfied to very dissatisfied. Flanagan's subjects were asked "How well are your needs and wants being met?" They responded for each area on a five point scale ranging from "very well met" to "not at all well met".

In roughly comparable areas, the percent of our subjects and of Flanagan's 30 year olds who responded in the two most favorable categories are shown in the Table.

While it would not be appropriate to conduct statistical tests on the differences between groups, the figures do suggest that quality of life may be lower for people with disabilities than for the general population. A future study could profitably survey a sizable and representative sample of disabled persons using Flanagan's methods to learn more about the quality of their lives on his 15 dimensions. These dimensions might also be used in addition to functional measures as a basis for comparing the outcome of patients who receive comprehensive rehabilitation with those who do not.

TABLE  
Percent of Persons in Top 2 Categories  
of Satisfaction Ratings

MINNESOTA STUDY	%	%	FLANAGAN STUDY
Employment .....	39	79	Work
Financial .....	48	74	Material well being
Social .....	68	73	Socializing
Sexual .....	40	84	Relations with spouse
Health .....	63	86	Health and personal safety



The opportunities that quality-of-life research offers to rehabilitation seem particularly timely now when legislation promises to open up vast new areas of service under the canopy of independent living. Not only will a large new population become eligible for services under the Vocational Rehabilitation Act, but also the range of approved services may be greatly extended. Yet appropriations will not provide a carte blanche. Difficult decisions about priorities will have to be made, and somehow the results of the new programs will have to be evaluated. Dollar savings resulting from deinstitutionalization and even some

vocational rehabilitation success will be important criteria. Comprehensive assessment of independent living programs need not depend entirely on the cost-benefit analysis for justification, however. If, as Rehabilitation Service Administration Commissioner Humphreys has said, "Independent living is an idea whose time has come," then the same must be said for the concept of quality of life. We have already demonstrated that rehabilitation medicine is cost effective, and now we may have a method for documenting its impact in terms of overall quality of life.

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### MINNPAC Distributes Funds — Encourages Continued Involvement

Filings for Legislative races closed July 15. MINNPAC Board members met July 24 to discuss candidates and authorize contributions in the various races. Chief attention was given to candidates running for seats now held by health committee members.

Emphasis now shifts to the local districts. "Physicians must continue their political involvement," said MINNPAC Chairman, L. Ashley Whitesell, Jr. M.D. According to Dr. Whitesell, cooperation from physicians in commenting on candidates provided valuable assistance to MINNPAC in considering disbursements.

MINNPAC members will be visiting with candidates in their home communities now through the election. Physician participation is strongly encouraged. If you are interested in a meeting with legislative candidates, contact the MINNPAC office and we will arrange a local visit.

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### Depression in a Medical Setting

Since the journal's acceptance of the Special Article, 'Depression in a Medical Setting', appearing in the June, 1980 issue, Dr. Russell Wilder, one of the article's contributors, died quite unexpectedly. Dr. Drucker and Dr. Heefner currently are co-medical directors of the Metropolitan Clinic of Counseling. Dr. Drucker maintains a clinical appointment at the University of Minnesota. Dr. Heefner maintains a part-time consulting position with the Section of Psychological Medicine, Department of Medicine, Minneapolis Veterans Administration Medical Center.



# Effect of Social Class on Recovery from Myocardial Infarction

## A Followup Study of 197 Consecutive Patients Discharged from Hospital

THOMAS E. KOTTKE, M.D.;\* DANIEL T. YOUNG, M.D.† and MARVIN M. McCALL, M.D.‡

The recovery of 197 selected myocardial infarction patients and the relationship of recovery to the patients' social class were investigated. Measures of death, reinfarction, exercise capacity by treadmill examination, anxiety level, and occupational status were used to evaluate the effect of social class on morbidity and mortality after myocardial infarction. The lower class patients tend to have poorer prognoses than the upper class patients. This may be an effect of comorbidity. Lower class patients could have benefited from interventions to increase adherence to medication regimens, including the removal of financial barriers to care.

SOCIAL CLASS MAY be a factor in a patient's recovery from myocardial infarction. Most studies on myocardial infarction recovery focus on physiological, rather than sociological factors. However, some investigators have reported on the effects of social class on recovery. Kitagawa<sup>1</sup> has documented that age adjusted death rates from coronary heart disease are highest among the lower social classes. Lower class telephone company employees have a higher risk of developing cardiac disease than do their higher class counterparts, according to Hinkle.<sup>2</sup> Physicians, Hrubec<sup>3</sup> noted, had a better prognosis after myocardial infarction than other groups of patients. Shapiro<sup>4</sup> and Kentala<sup>5</sup> found a negative effect of low social class on return to work, and Weinblatt<sup>6</sup> noted an interaction of education and ventricular arrhythmia on survival. This evidence from epidemiologic studies on patterns of infarction suggests that social class has an important influence on recovery from infarction. This paper discusses an investigation of the recovery of selected myocardial infarction patients and the relationship of recovery to the patient's social class.

### Methods

One hundred and ninety-seven patients consecutively discharged from a metropolitan hospital in North Carolina were re-evaluated at three months and one year after discharge from the hospital. These patients were required to meet the following criteria:

1. The patients must be under 65 years of age.
2. They can have no concomitant life-threatening illnesses.
3. The patients must be employed. If they are retired they must be able to perform activities of daily living and ambulate well.
4. The patients must meet two of the three following criteria for myocardial infarction:
  - a. history typical of myocardial infarction;
  - b. ECG changes of myocardial infarction; or
  - c. serum enzyme changes (CPK, LDH, SGOT) consistent with acute myocardial infarction.
5. The patients must be suffering from their first myocardial infarction or have gone back to full activity after a previous myocardial infarction.

The major purpose of this study was to test the effects of an in-hospital rehabilitation intervention consisting of risk factor education and supervised ambulation.<sup>7</sup> Although patient behavior patterns were influenced, the intervention had little effect on the outcome. For the evaluation of social class on recovery from infarction, the control and rehabilitation groups were aggregated and restratified by the five social strata of Hollingshead,<sup>8</sup> based on education and job

This project was supported in part by Grant #25P-20-437/4 from the Social Rehabilitation Service — Rehabilitation Services, Region IV, and from a State Grant 7501 from the Division of Vocational Rehabilitation Services, North Carolina Department of Human Resources.

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description. The principal investigator and other staff were not aware that the hypothesis regarding social class and its influence on recovery from myocardial infarction would be tested.

The study patients completed a risk factor knowledge assessment questionnaire and a physical activity questionnaire while in the hospital and at each of the two followup evaluations. A sub-maximal (80-90%) treadmill exercise test was administered at the three month evaluation, and an intervening history, a physical examination, an ECG, and a chest x-ray were taken at both the three month and one year evaluations. The principal investigator (DTY) performed all of the evaluations. Discharge medication records were obtained from the patients' charts, and medication use at the three month and one year evaluations was determined by patient report. If a patient had been hospitalized in the first year after the infarction for any reason, the medical record was searched for evidence of myocardial infarction using the study entrance criteria. A self-report anxiety questionnaire, the State-Trait Anxiety Inventory (STAI),<sup>9</sup> was mailed to each participant approximately eighteen months after infarction.

For this study, five measures were used to evaluate the effect of social class on morbidity and mortality after myocardial infarction: death, reinfarction, exer-

cise capacity by treadmill examination, anxiety level (as measured by the STAI), and occupational status. Univariate analyses were performed on the following groups of variables: demographic characteristics and medical history; acute infarction and hospitalization characteristics; treadmill exercise test performance; historical and physical examination characteristics, including work status, three months and one year after infarction; and emotional status after a convalescent period. Categorical variables were subjected to the chi-square test and continuous variables were subjected to analysis of variance tests. Covariance analysis was used to adjust for confounding by comorbidity and infarction severity in the analysis of return to work, death, and reinfarction patterns. Because of the small number of deaths and reinfarctions, death and reinfarction have been combined under the rubric of "new events" for the multivariate analysis. The effect of hypertension on new events received special attention because it is a treatable risk factor.

## Results

Although the mean age was not different across the five groups, women and blacks clustered in the lower strata. Also, lower classes tended to have more family disorganization as shown by higher rates of separated, divorced, widowed, and single subjects (Table 1).

**TABLE 1**  
**Demographic and Medical History Characteristics**

class	1	2	3	4	5	p
<u>Sex (n)</u>						
males	9	12	51	65	30	
females	0	0	9	9	12	<.05
<u>Race (n)</u>						
white	8	11	60	67	30	
black	1	1	0	7	12	<.001
<u>Age</u> ( $\pm$ S.D.)	53.3 $\pm$ 5.5*	51.1 $\pm$ 6.0	50.6 $\pm$ 6.8	50.9 $\pm$ 7.7	52.2 $\pm$ 8.2	NS
<u>Marital Status (%)</u>						
married	100	92	85	90	69	
separated	0	8	0	3	5	
divorced	0	0	10	3	10	
widowed	0	0	3	3	14	
single	0	0	2	1	2	NS
<u>Previous Hypertension</u> (%)	11	50	37	41	41	NS
<u>Previous Diabetes</u> (%)	0	0	12	10	21	NS
<u>Smoking History</u> (mean pack-years)	44.3 $\pm$ 27.2	31.5 $\pm$ 33.2	38.5 $\pm$ 25.6	43.3 $\pm$ 28.9	25.8 $\pm$ 22.1	<.025
<u>Knowledge Assessment Test</u> (% of items answered correctly)	86 $\pm$ 9	87 $\pm$ 9	82 $\pm$ 11	75 $\pm$ 20	60 $\pm$ 23	<.001

\*all continuous variables  $\pm$  S.D.



Smoking history and knowledge about cardiovascular risk factors were the only variables in the medical history that were significantly different among the classes (Table 1). The first and fourth classes had the largest tobacco consumption (44.3 and 43.3 pack-years, respectively) but there was no linear trend from highest to lowest class. The prevalence of documented hypertension and diabetes was not significantly different among the classes.

The hospital course (including severity of infarction by Norris index, and complications of shock and congestive heart failure) was also not significantly different for any of the social classes (Table 2).

At the three month evaluation, the classes showed a significant difference for the following variables: systolic and diastolic blood pressure, cardiothoracic ratio on Xray, and ponderal index (weight/height<sup>2</sup>) (Table 3). The proportion of patients smoking was not different among the classes. All five of the deaths occurred in the two bottom classes ( $p < .10$ ). The distributions of new infarctions determined by ECG alone (new Q-waves) or by history and enzyme levels were not significant. Although lower class patients tended to have more severe angina and congestive heart failure, these patterns were not statistically significant (Table 3). The proportion of hypertensive

patients was significantly greater in the lower than in the upper classes (Figure 1). All reinfarction patients were in the two lowest social classes. The pattern of new events was significantly skewed towards the lower social classes ( $p < .05$ ) (Figure 2). Exercise capacity on the treadmill test was approximately the same for all classes (Table 4).

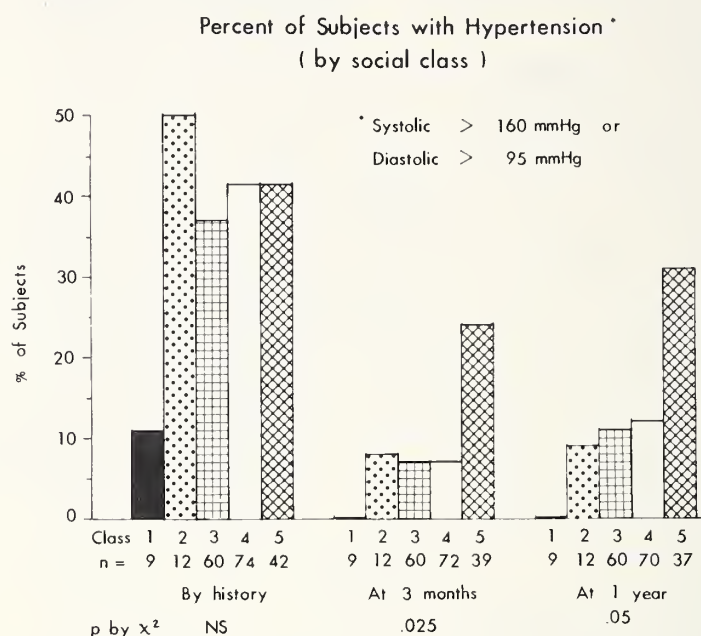


Figure 1

TABLE 2  
Acute Infarction Period Characteristics

class	1	2	3	4	5	p
<u>Initial Systolic Pressure</u>	136.6 ± 19.5	147.1 ± 25.2	136.5 ± 27.5	138.8 ± 23.7	139.6 ± 30.5	NS
<u>Initial Diastolic Pressure</u>	92.4 ± 14.7	94.4 ± 15.5	87.4 ± 15.1	90.3 ± 14.1	92.2 ± 18.0	NS
<u>Location of Infarction (%)</u>						
anterior transmural	55	34	28	26	24	
left bundle branch block	0	0	0	1	0	
inferior transmural	33	34	60	46	55	
anterior subendocardial	0	8	2	15	17	
inferior subendocardial	12	8	8	8	2	
other	0	16	2	4	2	NS
<u>Norris Index of Severity (short-term)</u>	5.03 ± 2.00	4.78 ± 2.15	4.87 ± 2.21	4.91 ± 2.20	5.15 ± 2.34	NS
<u>Shock in Hospital (%)</u>	11	8	0	4	7	NS
<u>Congestive Heart Failure in Hospital (%)</u>	44	17	18	23	29	NS
<u>Ponderal Index<sub>2</sub> (weight/height<sup>2</sup>)</u>	.034 ± .003	.036 ± .004	.037 ± .006	.037 ± .005	.038 ± .006	NS
<u>Discharge Systolic Pressure</u>	111.3 ± 22.0	113.0 ± 9.0	113.7 ± 16.1	120.6 ± 12.4	116.2 ± 15.8	NS
<u>Discharge Diastolic Pressure</u>	72.0 ± 12.4	73.8 ± 9.8	73.8 ± 11.3	73.2 ± 8.6	74.9 ± 10.2	NS
<u>Hypertensive<sup>1</sup> on Discharge From Hospital (%)</u>	0	0	10	1	2	<.10

<sup>1</sup>last recorded blood pressure greater than 160 mm Hg. systolic or 95 mm Hg. diastolic



At the one year evaluation, more of the lower class patients suffered from angina and congestive heart failure and were in higher New York Heart Association (NYHA) classes for the two conditions than upper class patients (Table 5). Although the distribution of new infarction by ECG alone was not significant, new infarction by the complete study criteria and deaths tended to be clustered in the lower classes. Uncontrolled hypertension remained skewed towards the lower classes (Figure 1). The clustering of new events in the lower classes also remained significant (Figure 2). Large cardiothoracic ratio was closely related to elevated blood pressure (Pearson's  $r = .55$ ,  $p < .001$ )

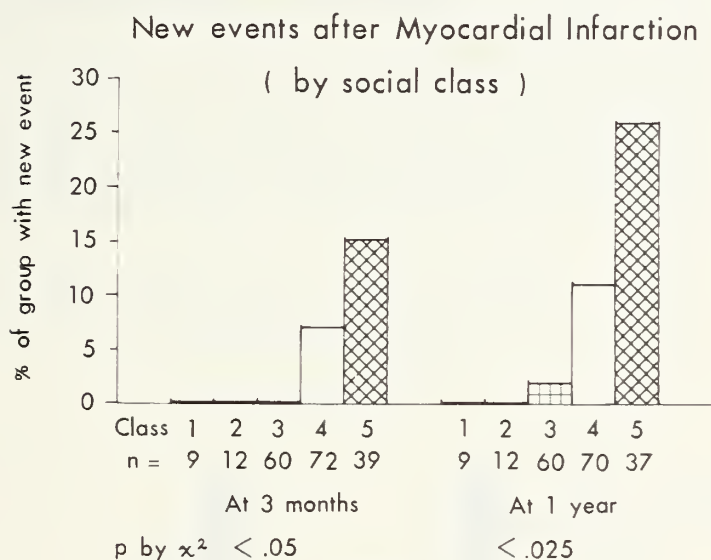


Figure 2

and was associated with low social class (Table 5). Neither ponderal index nor smoking behavior was associated with social class at the one year evaluation.

Anxiety towards the heart and life in general was significantly higher for the lower social classes (Figure 3). However, this effect was due mainly to the female subjects. After stratification by sex, the males did not

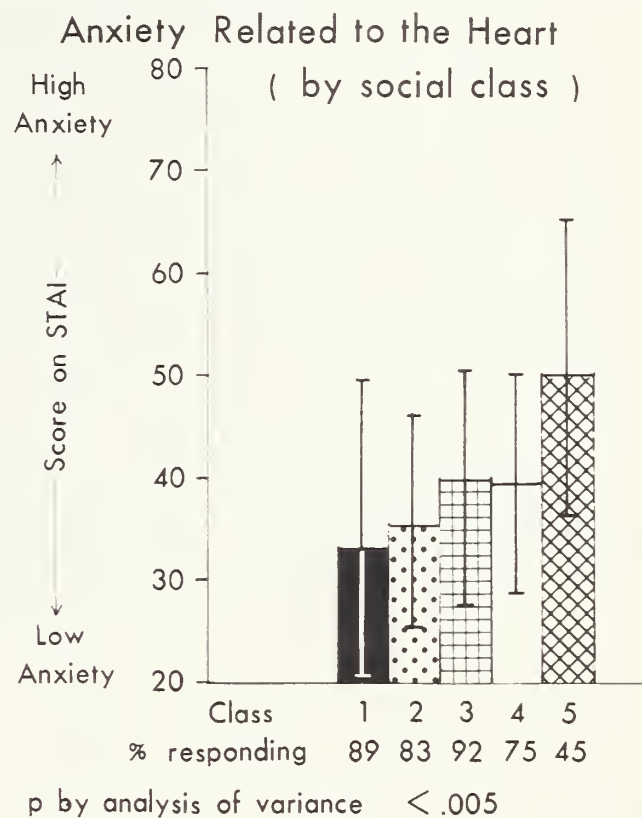


Figure 3

TABLE 3  
Characteristics at Three Month Evaluation

class	1	2	3	4	5	p
<u>NYHA Angina Class (%)</u>						
I	78	83	70	61	53	
II	22	17	18	30	29	
III	0	0	12	10	18	
IV	0	0	0	0	0	
V	0	0	0	0	0	NS
<u>NYHA Congestive Heart Failure Class (%)</u>						
I	78	92	73	76	66	
II	22	8	22	24	29	
III	0	0	5	0	5	
IV	0	0	0	0	0	
V	0	0	0	0	0	NS
<u>Nitroglycerine Use</u> (tablets/day if angina present)						
	0	0	2.2 $\pm$ 3.8	5.4 $\pm$ 8.4	12.4 $\pm$ 19.7	<.10
<u>S<sub>3</sub> Present (%)</u>						
	11	8	2	3	3	NS
<u>Systolic Blood Pressure</u>						
	127.2 $\pm$ 18.2	124.0 $\pm$ 14.1	131.0 $\pm$ 15.7	129.7 $\pm$ 16.9	143.8 $\pm$ 30.1	<.01
<u>Diastolic Blood Pressure</u>						
	82.6 $\pm$ 6.3	81.2 $\pm$ 11.0	82.4 $\pm$ 8.4	81.7 $\pm$ 9.7	87.5 $\pm$ 12.4	<.05
<u>Cardiothoracic Ratio</u>						
	.45 $\pm$ .05	.44 $\pm$ .04	.45 $\pm$ .03	.46 $\pm$ .05	.47 $\pm$ .05	<.05
<u>Ponderal Index</u> (weight/height <sup>2</sup> )						
	.034 $\pm$ .003	.036 $\pm$ .005	.036 $\pm$ .005	.036 $\pm$ .005	.038 $\pm$ .006	<.05
<u>Recurrent Infarction (%)</u> (by medical record)						
	0	0	0	4	8	NS
<u>Death (%)</u>						
	0	0	0	3	7	<.10
<u>New Q-Waves on ECG</u>						
	0	0	0	1	2	NS



have significantly different mean scores for anxiety among the classes.

Major activity status (return to employment for those previously employed, and return to other major pre-infarction activity for those not employed) at both evaluations was significantly poorer for the lower class patients than for the upper class patients. Only 35% of the lower class patients returned to major activities, while almost 90% of the upper class patients resumed these activities (Figure 4). Analysis of covariance revealed that severity of infarction was prognostic of return to activity only in the first three months after infarction. The interaction of occupational metabolic demand and severity of infarction did not clarify the patterns of activity at either evaluation. However, the relationship of low social class to poor activity status was statistically significant at both evaluations. This gap in activity status across social class widened with increasing severity of infarction (both  $p < .05$ ).

In a statistical model with new events (death and reinfarction) as the dependent variable, diabetes and severity of infarction are the two most important physical variables associated with a new event (both  $p < .01$  by the partial F-test). Although hypertension alone was not related to new events and the relationship of social class to a new event is not significant after adjustment for diabetes and severity of infarction, the interaction of hypertension and social class to a new event was significant (Table 6). That is, lower social class patients with hypertension had poorer prognoses than either upper class patients with or without hypertension or lower class patients without hypertension.

Reported patterns of prescription for digitalis and blood pressure medication were not different across the five social classes for any of the three time periods. Also, after adjustment for social class, whether a patient was a hospital staff clinic patient or a private patient did not influence the expectation of uncontrol-

led hypertension or a new cardiac event.

Although four of the thirty females (13.3%) died during the followup period while only five of the 167 males (3.0%) died ( $p < .05$  by chi square test), statistical adjustment for hypertension and diabetes revealed that this was an effect of comorbidity and not gender itself. There was no independent effect of race on survival.

### Discussion

Although an observational study lacks some of the power of a randomized clinical trial and the numbers of events are small, valid inference can be drawn from the data collected. Selection bias would not affect the study population, because all consecutive patients in a defined population who met the study criteria were enrolled until the study was filled. The outcome criteria: death, reinfarction, exercise capacity, anxiety level, and occupational status were all objective

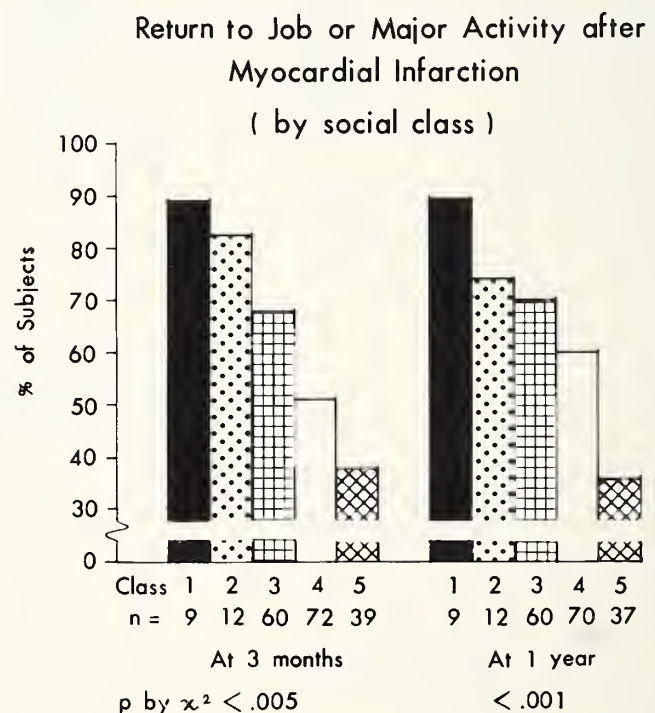


Figure 4

**TABLE 4**  
**Exercise Performance on Treadmill Test**

class	1	2	3	4	5	p
n of Tests	6	8	38	47	20	
% of Subjects Tested	67	75	63	65	51	
Maximum $\text{VO}_2$ Uptake (calculated)	$30.6 \pm 5.1$	$29.6 \pm 9.8$	$25.9 \pm 8.7$	$26.2 \pm 10.5$	$25.6 \pm 7.7$	NS
Maximum Heart Rate	$146.3 \pm 11.5$	$144.5 \pm 23.5$	$133.3 \pm 22.4$	$137.6 \pm 19.6$	$138.5 \pm 21.1$	NS



measurements that were not subject to bias in measurement or observation.

It is impossible to draw direct inference from the post-infarction data on those patients who died or had a new event. First, those patients who died were "lost to followup" for all followup parameters except survival, as no data are available on their condition immediately preceding their demise. Second, the data on those patients who have had a reinfarction are biased because they have received an additional intervention that the rest of the population has not received. However, the pre- and peri-infarction data, along with the data on those patients who did not have new events, can be used to draw inference about causes of morbidity and mortality.

Because the total number of events was small in the followup period, indices like risk-ratios and risk-differences cannot be calculated. However, statistical tests for variations from expected patterns can be applied. For all five measures (except possibly exercise capacity), the lower class patients, as a group, tend to have a poorer prognosis than the upper class

patients. Exercise capacity possibly was not different for the five groups because it was measured before the lower class patients began to deteriorate physically. The patterns of disability from angina and congestive heart failure among the classes that were not different at three months, but were markedly different at one year, support this hypothesis.

Although women in the lower classes reported more anxiety than women in the middle class (the study contained no women in the upper two classes), this same pattern did not exist for men. Two explanations seem plausible. First, there may have been no difference at any point in time among the five groups. Second, because emotional status was surveyed only 18 months after the event, any difference existing from the time of infarction may have disappeared by the time of the survey. Although women in the intervention group tended to have less anxiety than women in the control group, suggesting that education and exercise prescription reduce anxiety, further investigation probably would clarify the effects of social class on emotional response to myocardial infarction.

TABLE 5  
Characteristics at One Year Evaluation

class	1	2	3	4	5	p
<u>NYHA Angina Class (%)</u>						
I	100	83	61	72	49	
II	0	8	27	21	40	
III	0	0	7	7	11	
IV	0	0	0	0	0	
V	0	0	0	0	0	<.05
<u>NYHA Congestive Heart Failure Class (%)</u>						
I	89	83	76	77	43	
II	11	8	15	12	41	
III	0	0	2	0	5	
IV	0	0	0	0	0	
V	0	0	0	0	0	<.001
<u>Nitroglycerine Use (tablets per day if angina present)</u>						
	0	1.5 ± 2.1	6.8 ± 14.7	7.2 ± 14.1	2.7 ± 3.9	NS
<u>S<sub>2</sub> Present</u>						
	11	0	0	3	5	NS
<u>Systolic Blood Pressure</u>						
	133.9 ± 15.8	129.1 ± 17.4	134.5 ± 20.8	136.8 ± 17.8	147.3 ± 26.0	<.05
<u>Diastolic Blood Pressure</u>						
	83.9 ± 6.0	83.6 ± 9.5	82.9 ± 9.6	85.8 ± 9.5	89.6 ± 12.6	<.05
<u>Cardiothoracic Ratio</u>						
	.46 ± .05	.44 ± .05	.46 ± .04	.47 ± .04	.49 ± .04	<.025
<u>Ponderal Index, (weight/height<sup>2</sup>)</u>						
	.035 ± .003	.036 ± .005	.036 ± .005	.037 ± .005	.038 ± .006	NS
<u>Recurrent Infarction (%) (by medical record)</u>						
	0	0	2	6	14	NS
<u>Deaths (%) (cumulative)</u>						
	0	0	0	5	12	<.10
<u>New Events (%) (deaths or new MI)</u>						
	0	0	2	11	26	<.025
<u>New Q-Waves on ECG (%)</u>						
	0	0	2	3	7	NS



As in Kentala's and Shapiro's studies, the lower class patient did not return to major activity as often as the upper class patient. This distinction was most pronounced for those patients with severe infarctions. Although mean metabolic demands did not vary among the classes, the lower class patient probably did not return to work because the peak metabolic demands could not be tolerated. The differences for rates of return to work were much greater for subjects with severe infarction than for those with mild infarction, thus supporting this assumption. However, even after statistical adjustment for severity of infarction, social class remained important in predicting work status. Employer attitudes or the lower class patient's lack of incentive to return to work may have influenced the work status. The definitive answer cannot be obtained from this study.

When all cardiac events, death, and reinfarction are treated together, the lower class patient apparently suffers from an excess burden of disease. This appears not to be effect of class itself, but rather an effect of comorbidity. In the analysis of covariance model, the most important variables in predicting whether a patient will have a new event are a past history of diabetes, a severe infarction, and the interaction of social class and a history of hypertension. Because hypertension treatment reduces the incidence of stroke<sup>10</sup> a randomized trial of hypertension treatment to reduce the incidence of reinfarction is no longer ethical. Burggraf,<sup>11</sup> Lundman,<sup>12</sup> and Vedin,<sup>13</sup> however, have found that a history of hypertension was

associated with poor post-myocardial infarction prognosis. Weinblatt<sup>6</sup> did not find this to be true. In this study, patients in the lower social classes had significantly more uncontrolled hypertension at both followup evaluations than the patients in the upper classes. The presence of uncontrolled hypertension in lower class patients without events, and the importance of the interaction of social class and history of hypertension in predicting a new event, may justify the conclusion that the lack of hypertension control was responsible for some of the lower classes' excess of new events.

Because, in many studies, adherence to medication maintenance is the major obstacle to the successful treatment of hypertension, problems with adherence may have contributed to the increased morbidity and mortality in the lower class patients. Financial barriers to medical care compounded by North Carolina's difficulty with the administration of their Medicaid program may have decreased adherence at the time of this study.<sup>14,15,16</sup> Weinblatt's patients were enrolled in a prepaid program and did not face financial barriers to care. The study data suggest that the lower class patients could have benefited from interventions to increase adherence to medication regimens, including the removal of financial barriers to care.

## Conclusions

Patients in the lower classes appear to have a poorer prognosis after their first myocardial infarction than

**TABLE 6**  
**The Role of Social Class-Hypertension Interaction on Explaining the Pattern of New Cardiac Events**

Dependent Variable: New Cardiac Events (Death or Reinfarction)						
<u>Analysis of Variance</u>	<u>d.f.</u>	<u>Sum of Squares</u>	<u>Mean Square</u>	<u>R<sup>2</sup></u>	<u>F</u>	<u>P</u>
Regression	7	3.235	0.462	.22	7.33	<.001
Residual	181	11.410	0.063			
Independent Variable: Social Class-Hypertension Interaction (Cross-product term)						
	<u>d.f.</u>	<u>partial-F</u>	<u>P</u>			
	4	2.5	<.05			
Concomitant (confounding) Variables:						
	<u>d.f.</u>	<u>partial-F</u>	<u>P</u>			
Severity of Infarction (by Norris Index)	1	33.1	<.001			
Presence of Diabetes	1	6.6	<.01			
History of tobacco smoking (in pack-years)	1	2.4	NS			

Legend: Even after statistical adjustment for possible confounding effects of severity of infarction, presence of diabetes, and history of smoking by analysis of covariance, social class-hypertension interaction remained important in explaining the pattern of new cardiac events.



patients of the upper classes. The following indicators support this observation:

1. Lower class patients suffered from higher rates of new cardiac events (death and reinfarction). Uncontrolled hypertension may be one of the factors responsible for this observation. The lower class patient might benefit from maneuvers, including removal of financial barriers to care, that increase adherence to medication regimens.
2. Lower class patients returned to preinfarction major activity at a lower rate than upper class

patients. This relationship persisted after adjustment for severity of infarction, but was most pronounced in patients with severe infarctions.

3. Patients in the lower classes reported more anxiety than patients in the upper classes.

The results of this study also suggest that when investigators are testing modalities for intervention and treatment of myocardial infarction and other forms of heart disease, the confounding effects of social class must be considered so that the results are not biased by these factors.

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## Minnesota Radiological Society

Fall Meeting  
September 6, 1980  
Minnesota Club  
317 Washington  
St. Paul, Minnesota

10:00 A.M. — 12:00 Noon Business Meeting  
12:00 noon — 1:30 P.M. Luncheon (Reservations Required)  
Radiology Residents guests of the Society  
Exhibit: Diagnostic Ultrasound — Daryl P. Williamson, M.D., St. Paul  
1:30 P.M. — 4:30 P.M. Scientific Program

Theme: Interventional Radiology

1:30 P.M. Percutaneous Transluminal Angioplasty — Ronald E. DeCesare, M.D., Minneapolis  
2:00 P.M. Percutaneous Biliary Decompression — Gerald R. May, M.D., Rochester  
2:30 P.M. Percutaneous Nephrostomy — Robert P. Miller, M.D., Donovan B. Reinke, M.D., Minneapolis  
3:00 P.M. Application of Total Lymphoid Irradiation for Organ and Marrow Transplantation, Tae Kim, M.D., Minneapolis.  
3:45 P.M. Forty-Fifth Carman Lecture — "Percutaneous Needling of Abdominal Tumors and Abscesses" — Joseph T. Ferrucci, Jr., M.D. — Boston, Massachusetts  
4:30 P.M. Reception

Contact: John B. Marta, M.D., 125 W. College Ave., St. Paul 55102.



## Physiatrists and Their Careers

A Case in Point

GARY T. ATHELSTAN, PH.D.\*

**The Commission on Education in Physical Medicine and Rehabilitation sponsored a study of the career development of all of the physiatrists in the United States. Some findings of the Commission's research, the features of a "typical physiatric career", and the differences between physiatrists and other physicians are discussed. Strong Vocational Interest profiles of physiatrists and a brief case study of a physiatrist are reviewed.**

**T**WELVE YEARS AGO the Commission on Education in Physical Medicine and Rehabilitation sponsored a study of the career development of all of the physiatrists in the United States.<sup>1</sup> These careers and characteristics, such as interests and values, were investigated because the Commission was concerned about the recruitment of physiatrists. Fifteen years ago, the shortage of qualified physiatrists was even more acute than it is now, and the Commission was seriously considering a major recruitment campaign to attract more people into the field. The Commission was persuaded to try, first, to learn something about the characteristics of people already in the field and how they happened to enter Physical Medicine and Rehabilitation.

There seemed to be a consensus among the Commission members and other physiatrists that physiatrists are different in some important respects from other physicians. They are more interested in comprehensive, long-term patient care and the humanitarian orientation they share with other physicians is of a distinctive quality. No good evidence for this was available, however, so the Commission initiated its study of physiatrists. The Commission believed that objective knowledge of the career patterns of physiatrists and of the factors that influence their career decisions could be valuable in directing recruitment efforts. Such knowledge could help select appropriate target groups and suggest advantageous times or methods for exposing potential recruits to information about the field.

The study that the Commission undertook was very comprehensive, including 856 subjects, or almost every single person in the country whose identity as a

physiatrist could be confirmed. Detailed information was gathered from these people concerning their educational and career backgrounds, how they were first exposed to the practice of Physical Medicine and Rehabilitation, what attracted them to the field, and what sources of satisfaction they currently found in it. In addition, they provided details on their employment settings and professional activities, and they filled out the Strong Vocational Interest Blank.

Some of the findings of that research will be briefly reviewed and some of the features of a "typical physiatric career" will be described. The difference in interests between physiatrists and other physicians and how these differences may be reflected in their careers will be demonstrated. These points will be illustrated by reviewing a few interest test profiles, and through a brief case study.

### Interest Test Profiles

Physiatrists in this study were asked what attracted them to this specialty and what they found most satisfying about being in it. Their responses emphasized the broad scope of the field, the opportunity to have extended and intensive patient contact, and the "whole man" approach to treatment which is characteristic of rehabilitation. A few people, of course, mentioned such things as the hours and working conditions, but most of the factors which seemed important have to do with the content of the field and the nature of its practice. This is very clearly reflected in the measured vocational interests of physiatrists.

One instrument used to measure job preference is the Strong Vocational Interest Blank. This test presents a number of statements describing activities, occupations, school subjects, and characteristics of people, to which a person responds, "like", "indifferent", or "dislike". Then, all of the individual's responses are

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TABLE  
Mean SVIB Scores on 55 Scales for Male Physiatrists, Physicians-in-General, and Psychiatrists

	Physiatrists (N = 489)	Physicians-in-General (N = 500)	Psychiatrists (N = 398)
Physical therapist	39	35	35
Dentist	31	41	31
Osteopath	37	44	37
Veterinarian	24	32	23
Physician	42	50	43
Psychiatrist	40	38	50
Psychologist	37	33	44
Biologist	38	39	40
Architect	27	32	28
Mathematician	27	27	29
Physicist	25	27	25
Chemist	33	35	34
Engineer	27	32	28
Production manager	28	29	26
Army officer	24	19	20
Air Force officer	30	25	27
Carpenter	17	21	14
Forest service man	17	20	14
Farmer	27	33	25
Math. phys. sci. teacher	32	30	29
Printer	23	26	20
Policeman	18	20	15
Personnel director	26	21	30
Public administrator	38	29	39
Rehabilitation counselor	33	27	36
YMCA secretary	24	17	21
Social worker	33	24	37
Social science teacher	27	23	26
School superintendent	28	22	29
Minister	28	20	26
Librarian	34	28	34
Artist	28	33	30
Music performer	38	36	37
Music teacher	31	25	29
C.P.A.	25	25	25
Senior C.P.A.	18	18	15
Accountant	18	15	13
Office man	20	20	15
Credit manager	27	22	25
Chamber of Commerce	31	25	30
Business education teacher	26	21	24
Purchasing agent	22	25	20
Banker	19	22	18
Pharmacist	25	32	25
Mortician	24	29	24
Sales manager	19	22	20
Real estate salesman	26	30	27
Life insurance salesman	23	26	24
Advertising man	25	29	28
Lawyer	32	35	36
Author-journalist	30	33	34
President-manufacturing firm	18	25	22
Specialization level	29	39	52
Occupational level	60	60	62
Masculinity-femininity	44	47	45



compared with the responses of people in selected occupations. The more similar a person's responses are to those of people in a given occupation, the higher will be the person's score on the scale for that occupation. The average score of any occupational group on its own scale is 50 (for example, physicians will average 50 on the physician's scale); the average score on a scale of people not in that occupation is about 25.

Scores on the Strong Vocational Interest Blank do not directly measure interest in a given occupation and they do not measure other qualifications such as ability. However, they are highly predictive of vocational behavior. People tend to enter those occupations for which they have high scores (that is, about 45 or above), and they tend not to choose, or to move out of, those occupations for which they have low scores (25 and below). The Strong Vocational Interest Blank has been used in a number of studies of medical interests (Figures 1 and 2).

Physiatrists, as a group, score quite a bit lower than other physicians on the scales for biological or

scientific fields that have restricted interpersonal contact or are technical in nature. Examples are the scales for pharmacists, dentists, veterinarians, architects, and engineers. Physiatrists score considerably higher on the scales for occupations involving social service and extensive contact with people: for example, the scales for physical therapists, psychologists, social workers, teachers, ministers, and public administrators. In fact, the interests of physiatrists somewhat resemble those of psychiatrists. This is not at all surprising, in view of the strong psychosocial and service orientation often found in this field. Also, the practice of physiatry is similar in some respects to that of psychiatry, and the interests of people engaged in similar activities should not differ greatly (Figure 3).

The interests of residents in Physical Medicine and Rehabilitation were studied separately. Their scores differed from those of other physicians in the same direction as did the certified physiatrists, but even more markedly. Apparently the younger people in the field are coming in with an even stronger social service

NCS PROFILE — STRONG VOCATIONAL INTEREST BLANK FOR MEN — COUNSELOR'S COPY

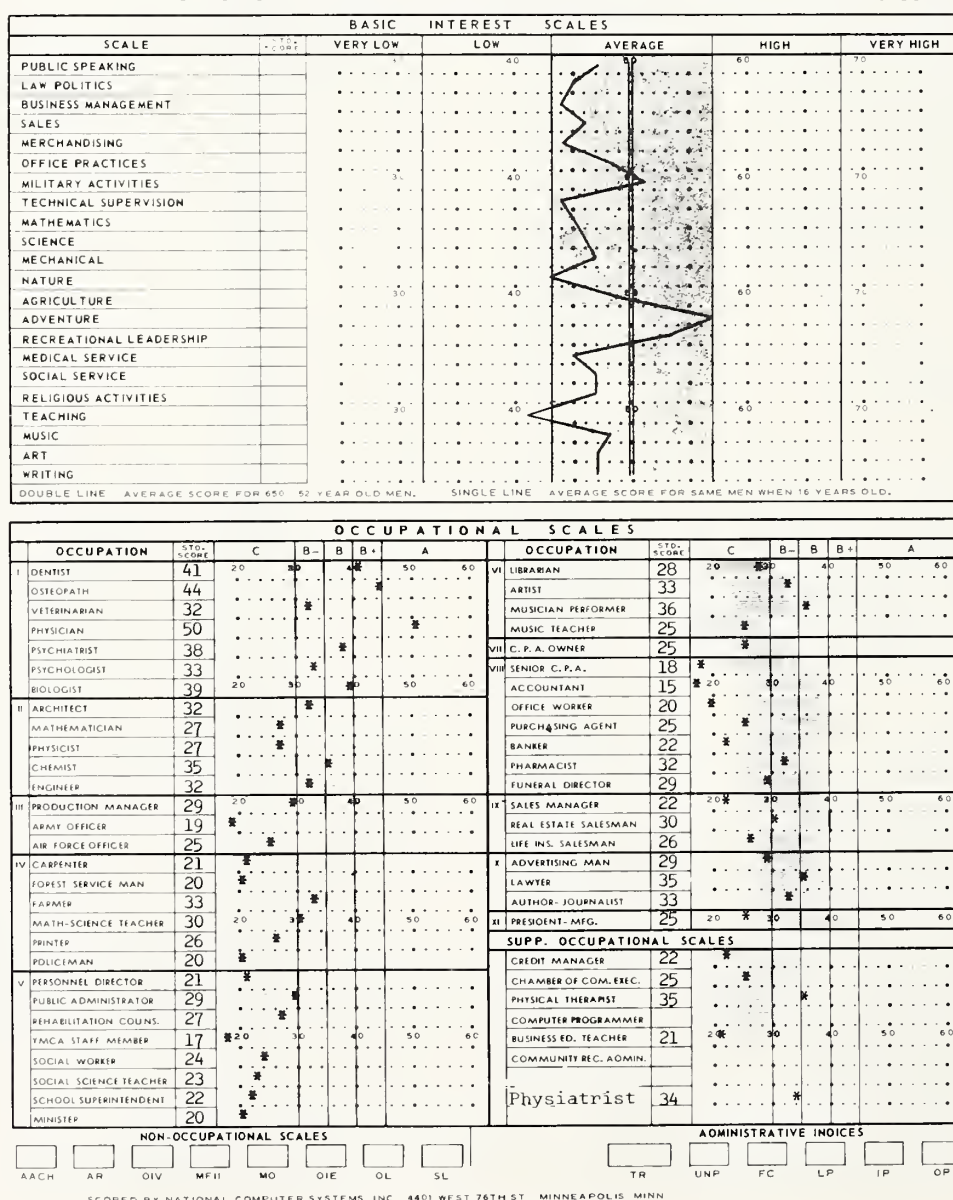


Fig. 1 — Physicians-in-General



# PHYSIATRISTS AND THEIR CAREERS — ATHELSTAN

orientation, and fewer interests shared with people in scientific and technical fields, than some of the established members of the specialty. To a degree, this finding reflects the history of the field. Since the beginnings of this specialty were in something akin to medical physics, it is not surprising that many of the early entrants to Physical Medicine and Rehabilitation would have interests consistent with their involvement in the physical sciences and other "basic science" kinds of activities. The growing emphasis in recent years on the psychosocial aspects of rehabilitation has produced a change in the nature of practice in this field. As a result, the specialty now tends to attract a somewhat different kind of resident, whose interests are consistent with this trend.

Recent work in such places as the University of Rochester in New York, Children's Orthopedic Hospital in Seattle, and at Ohio State University, strongly confirms these early findings. One recent study found strong similarities between the interests of residents in Physical Medicine and Rehabilitation and

residents in Family Practice.<sup>2</sup>

In examining the professional activities of physiatrists, a number of findings were quite congruent with the interest test results. For example, more than half of the physiatrists spend at least part of their time in an academic setting. Teaching is an important activity for a large proportion of the people in this field, even for those who are not primarily in academic settings.

The average physiatrist also reports being involved in a wide variety of professional activities. Over 70 percent report that their time is devoted to a combination of at least four major activities, usually involving direct patient care, teaching, research, and administration. Apparently the "pure" physiatrist is a consulting specialist in an academic setting. Despite this, however, the heavy clinical emphasis of this specialty is evident in frequent reports of very substantial commitments to patient care.

Considering these findings on the activities of physiatrists in relation to the Strong Vocational Interest Blank should enable a physiatrist's career to be

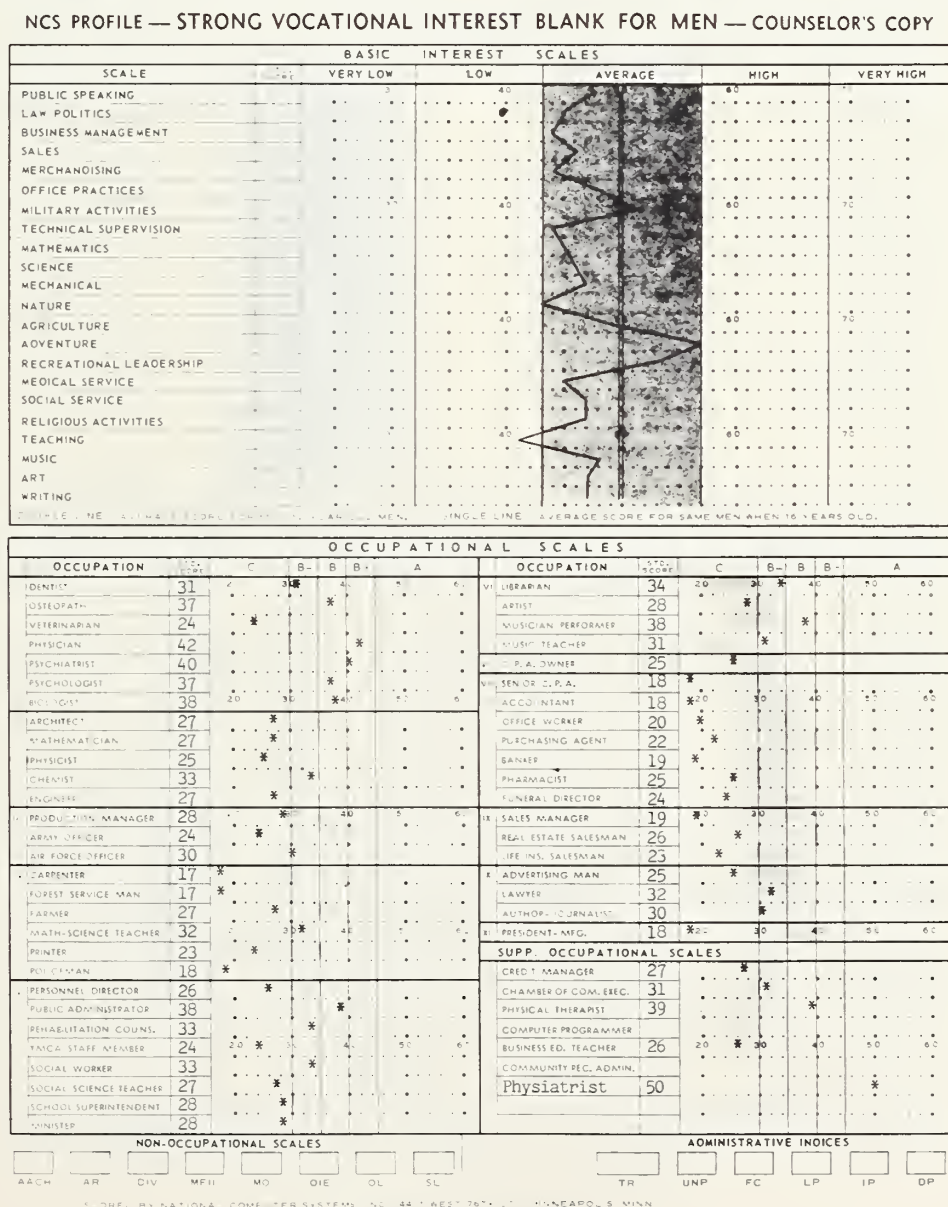


Fig. 2 — Physiatrists.



# PHYSIATRISTS AND THEIR CAREERS — ATHELSTAN

“mapped” from his interest test results. A sample profile can be used to demonstrate this relationship (Figure 4).

The first thing a vocational psychologist does in evaluating the profile of an individual is to look at the extreme scores. The high points are considered particularly important, since they will generally determine the positive directions in which a person’s career might move. The scores on the biological science scales clearly could belong to a physician. The scores on all of the scales relating to medical science are rather high. The physician’s scale actually has the highest score of the occupational scales. Such high interest scores are usually characteristic of administrators in a field. Several of the other scores in this group are very close to 50, which is the average for people in those occupations. It might be instructive to briefly examine a few of those groups.

The *osteopath* scale was based on 585 osteopaths in full-time practice. A high score on this scale usually goes along with an interest in clinical practice.

The *psychologist* scale was based on over 1,000 psychologists, most of whom were in academic settings. A large number were actually specialists in experimental psychology. A high score on this scale is often taken as an indication of research interests.

A high score on the *biologist* scale shows not only a shared interest in the content of biology; this scale is also judged to reflect research interests. The sample numbered 342 people all holding advanced degrees other than the M.D., all of whom were listed in American Men of Science. Fifty-four percent of them were teachers and 34 percent were researchers.

The remainder of the profile reveals high scores on the scales for physicists and chemists, which might reflect not only an interest in research, but probably a particular kind of research. If this person were involved in medical research, one might expect much of it to have a rather strong basic science flavor, quite possibly with an emphasis on physiology.

Going down the profile, a smattering of very moderate elevations on the social-service scales may

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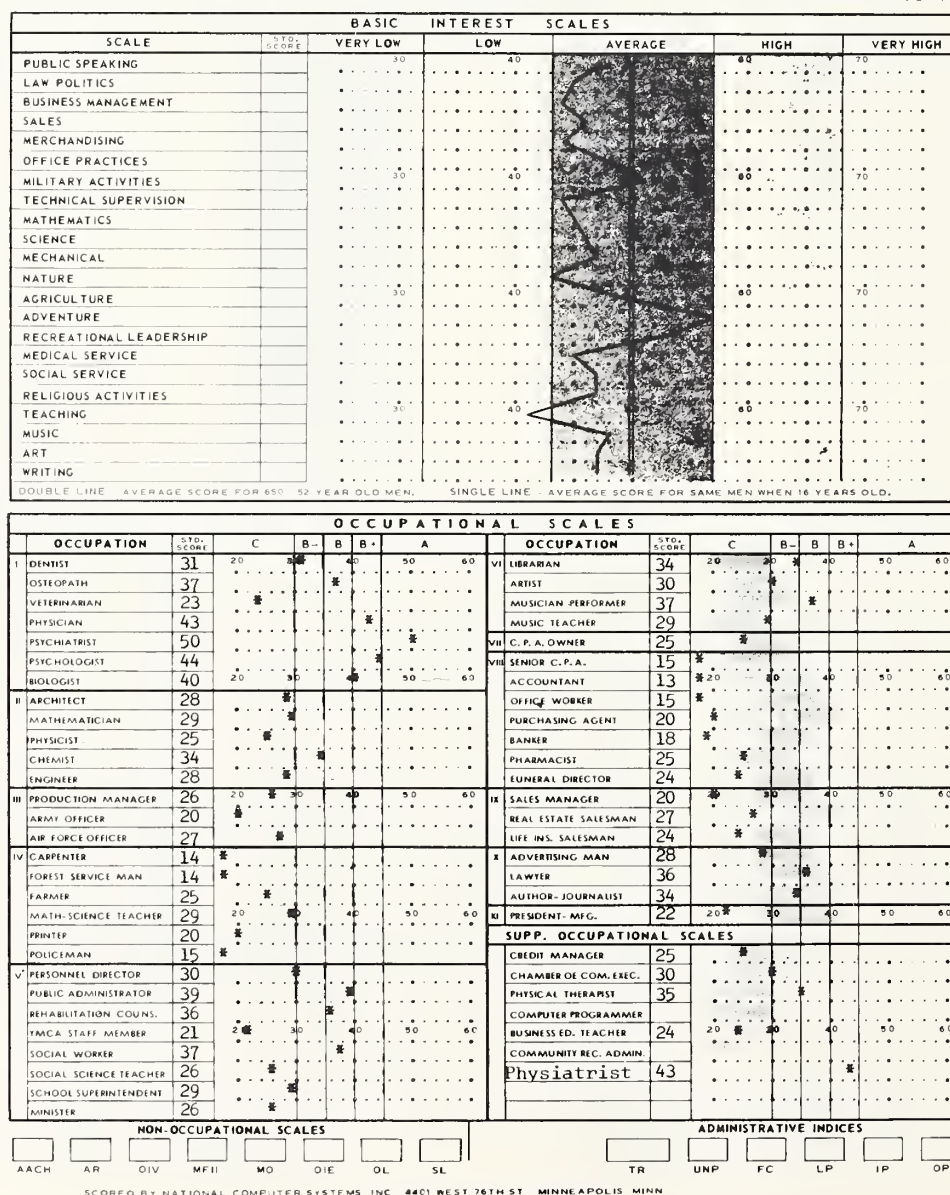


Fig. 3 — Psychiatrists.



# PHYSIATRISTS AND THEIR CAREERS — ATHELSTAN

suggest that this person's medical practice would not *ignore* the psychosocial aspects, but might tend to place greater emphasis on the physiological and physical aspects.

On the right hand side of the profile there are no outstandingly high scores, but a number of strikingly low scores, suggest the possibility of an active dislike for business detail activities. If a person like this were responsible for the financial aspects of a private practice or a program of any sort, one of two things would happen: either his budgets or finances would always be in a mess, or he would hire other people to take care of all of the financial details.

A little farther down this side of the profile is a slight elevation on the scale for lawyers. This, taken together with the indicated liking for public speaking, law, and politics, may indicate some taste for the negotiating and "give and take" of the political process.

The score of 51 on the physiatrist scale would be right on target for a member of this specialty.

Finally, two remarkably high scores appear on "special scales". The very high academic achievement score goes along with an unusual degree of interest in academic activities. Such people tend to be very good students, that is, to earn good grades and to enjoy reading, writing, and acquiring new knowledge. They often tend to accumulate advanced degrees.

The OL, or occupational level scale, is believed to measure something like a person's occupational aspiration level. The average for professional men on this scale is about 60, so this particular score is at about the 75th percentile for professional men. People with such scores tend to be in positions of leadership within the field, almost always in academic settings, and many of them are heads of academic departments.

Knowing something about the distinctive nature of Physical Medicine and Rehabilitation and the history of the field, and also knowing how both the content of the specialty and its history might be reflected in the interests of physiatrists, a hypothetical picture of the

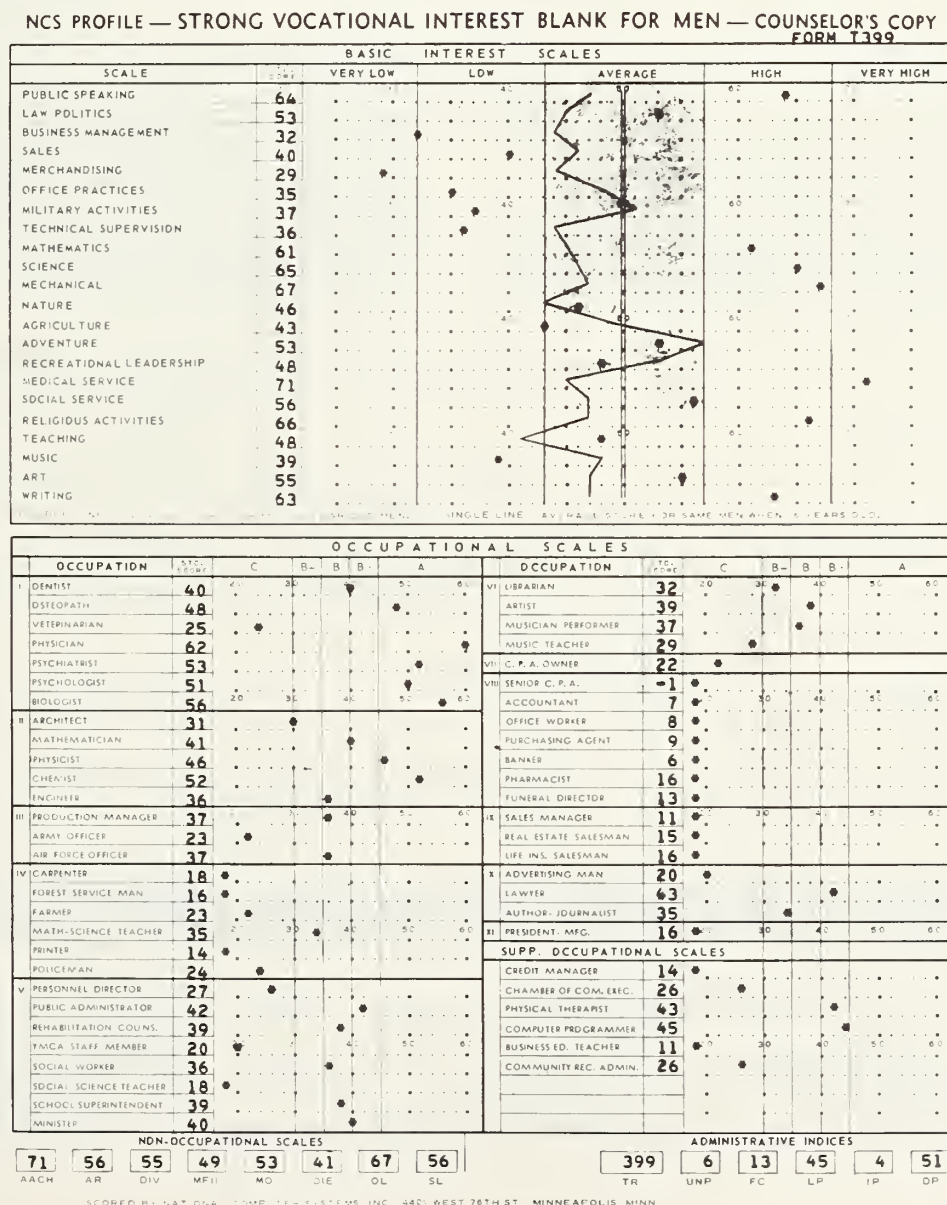


Fig. 4 — A sample physiatrist's profile.



career of a person like this could be constructed. Such a career might have started out with a very strong focus on research in the biological sciences. This person probably would have been a very good student and highly motivated to work toward one or more advanced degrees.

This person probably would become deeply involved in both research and teaching. Over time, there could be a gradual increase of interest in the psychosocial aspects of medicine, both in terms of research and practice.

Because of the high occupational level score, this person would be expected to strive for leadership,

some of which might be demonstrated through writing and publication, the remainder perhaps through the political process. It would not be surprising if such a person were to become a leader of considerable stature and eventually celebrated and honored for the way in which his interests were expressed through the course of a remarkable career.

#### Acknowledgment

My thanks to Dr. Kottke for his willingness to share his very interesting interest profile with us. It is always gratifying to obtain data that so strongly support one's research hypotheses, and even more so to find an individual case that so well represents an entire sample.

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*Myotonometry — Halpern et al. (page 575).*

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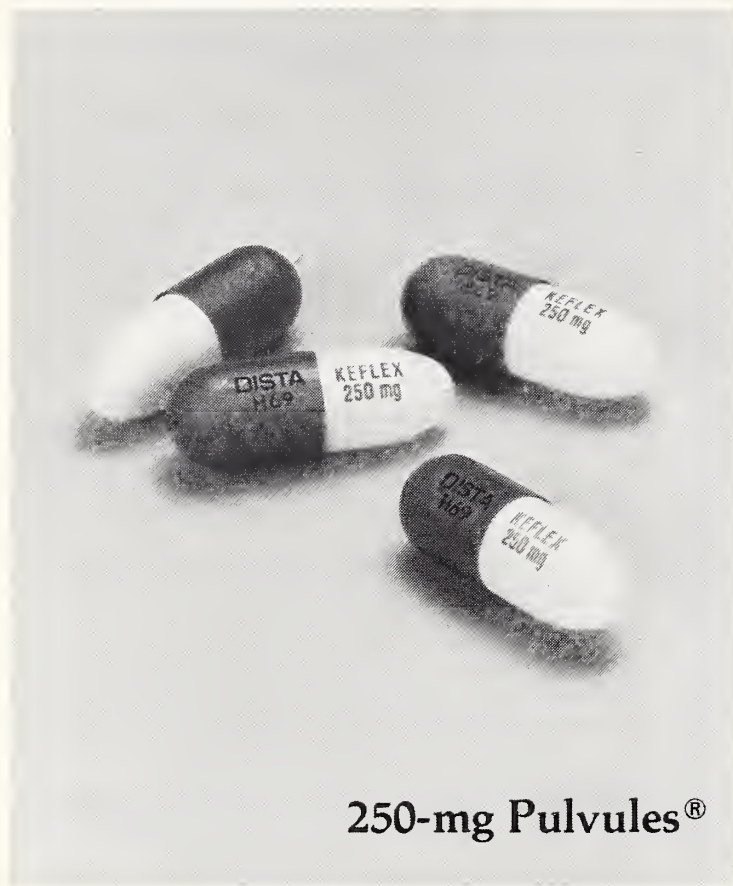
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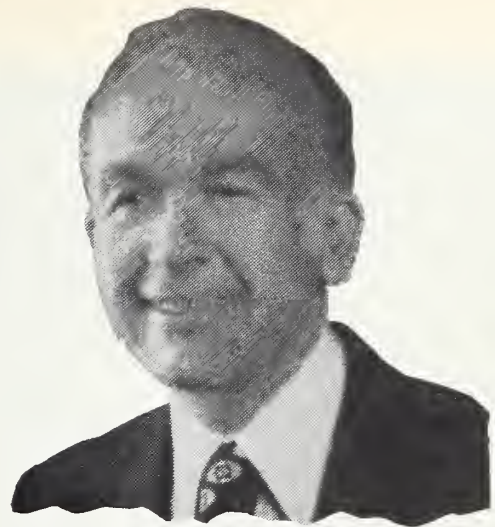
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# President's Letter



## Communication

"Communication" is a current buzz word. Despite this, it is important. If one stops to think about it, many of the problems that plague all of us are related at least in part to faulty communication.

As physicians we daily see patients who haven't followed our recommendations. Many times this is because they didn't understand them. These instances represent communication failure. Sometimes we have made recommendations to them that they cannot accept. These too may represent a failure in communication, for communication represents listening as well as speaking.

Communication also involves observing. Patients and others often send us communications by means of facial expression and body language. We communicate with them in the same way.

Almost daily most of us experience communication failure with colleagues and assistants. How much time could be saved and how much frustration alleviated if we were better communicators?

Communication, of course, is carried on in writing and print. Each order we write on a hospital chart is a communication. No one needs to be reminded how this method of communication breaks down at times.

This journal, others like it, newspapers, and books all deal primarily with communication. Although the authors and reporters strive for good communication, all too often the messages, scientific or otherwise, are unclear or confusing.

Communication inadequacies abound in our family and social relationships as well. I suspect much marital discord, many family quarrels, and even many divorces could be avoided if we were better able to communicate with each other. Professional misunderstandings and estrangements are frequently rooted in poor communications, in my experience.

Undoubtedly some have more natural ability to communicate than others; however, most of us could improve our abilities. We could learn to listen and observe better. We could delay our replies until we were quite certain what the other person meant, asking questions if necessary. We could phrase our responses and instructions carefully, in a calm manner using easily understood language. We can repeat, elaborate, and question to be certain our message is understood.

We all can and should strive to "communicate" better!

A handwritten signature in dark ink, reading "John K. Meinert M.D." with a stylized flourish at the end.

John K. Meinert, M.D.  
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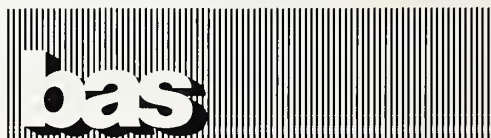
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The significant contributions of many individuals and organizations made my election to the AMA Board of Trustees a reality.

I know that without this generous giving of time and/or financial resources, my campaign would have been impossible.

Thank you for your support and confidence in me. Whenever you have opinions or information you wish to share, I want you to feel free to contact me. I will need your input to be an effective Trustee.

I will be working hard to represent you and to earn your continuing confidence and support.

With heartfelt thanks.

A handwritten signature in dark ink, reading "Bob Kelly". The signature is written in a cursive, slightly informal style.

Robert T. Kelly, M.D.  
Member, AMA Board of Trustees

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## Pre-School Medical Survey of Vision and Hearing

Mrs. Chauncey M. Kelsey

As a result of the Cabaret Medical Benefit Concert on July 9, 1980 at Orchestra Hall, there are funds to continue the Pre-School Medical Survey of Vision and Hearing program. A significant number of members of the MMA Auxiliary continue to support the program and to volunteer as screeners and demonstrators in screening the four-year-olds for possible vision and hearing problems. It is possible to continue this volunteer, medically-oriented program in conjunction with the State Pre-School Screening providing there is proper cooperation with the other agencies. Since the MMA Auxiliary has discontinued endorsing the PSMSVH as its one and only state program, there has been a considerable loss of volunteers from the County Auxiliaries. However, in the annual reports for 1980, about one-third of the County Auxiliaries stated a continued active participation in this program. In the Roseville #623 district, for example, there were six Auxilians who worked as volunteers one day each week from January through April, 1980 to screen the four-year-olds. In the Metropolitan Day Care Centers, several thousand children have been screened this year. In Minneapolis, teams of Auxilians have screened three- to five-year-olds. It has become much more difficult to recruit volunteers.

Of great value are public relations. Significant promotional strides have been possible through publications and by means of booths made available by the MMA and the Minnesota Academy of Family Physicians. Each year the auxiliary members staff the booths and provide current information as well as receive suggestions and comments from the medical doctors.

The Committee of the Cabaret Medical Benefit Concert appreciates and thanks those who supported the fund-raising event. The profit exceeds \$26,000.



Robert T. Kelly, M.D. (center) newly elected member of the AMA Board of Trustees with William E. Jacott, M.D. (left), Vice Chairperson and John J. Regan, M.D. (right), Chairperson, Committee to Elect Robert T. Kelly, M.D. Not pictured is Robert S. Flom, M.D., Vice Chairperson and Treasurer of the Committee.



# Prenatal Diagnosis of Sacrococcygeal Teratoma by Ultrasound

RICHARD P. BENDEL, M.D.\* and GORDON L. ALEXANDER, JR., M.D.\*

On an ultrasound study obtained at 30 weeks gestation because of uterine size larger than expected for dates, a 10 cm. complex mass was found arising from the caudal pole of the fetus. A prenatal diagnosis of sacrococcygeal teratoma allowed selection of cesarean section as the mode of delivery and appropriate preparations by the neonatologists and pediatric surgeons resulting in an excellent outcome for mother and baby.

**T**HE PRENATAL ULTRASOUND diagnosis of various congenital anomalies is being reported with increasing frequency. This report presents a case of a sacrococcygeal teratoma in which the prenatal diagnosis by ultrasound facilitated appropriate obstetrical management decisions.

## Case Report

A 23-year-old white woman, primigravida, was seen for her initial prenatal examination at nine weeks gestation by dates and size. For the preceding three weeks, because of a urinary tract infection, she had been taking a combination drug containing sulfisoxazole and phenazopyridine (Azo-Gantrisin®). This was discontinued. A drug containing doxylamine succinate and pyridoxine hydrochloride (Bendectin®) was prescribed for nausea. Because of uterine size larger than expected at 30 weeks gestation by dates, an ultrasound study was obtained and showed a fetal biparietal diameter at the

fiftieth percentile for 32 weeks gestation. Also noted was a large mass arising from the caudal pole of the fetus (Figure 1). This mass was partially solid and partially cystic (Figure 2). Two weeks later, a repeat ultrasound showed appropriate growth of the fetal head. The complex mass extending from the sacrococcygeal region of the fetus was measured at  $9 \times 10$  cm. A fetogram showed a normal fetal skeleton, and no evidence of calcification in the mass. Because it was both cystic and solid, and because of its anatomic location at the caudal pole of the fetus, the presumptive diagnosis was a sacrococcygeal teratoma. Since soft tissue dystocia with laceration and possible hemorrhage secondary to a traumatic delivery is a real possibility in these cases, the decision was made to deliver the baby by cesarean section. Shortly after the second ultrasound, the patient presented in active labor. A low segmented vertical cesarean section was done delivering a 2580 gram female infant with Apgar scores of six and seven at one and five minutes. The infant had a  $9 \times 9 \times 12$  cm. mass overlying the coccyx and distorting the perineum (Figure 3). The patient was transferred to the Newborn Intensive Care Unit and respiratory status stabilized. An evaluation for associated anomalies was done and none were found. Surgical excision of the

\*Department of Obstetrics and Gynecology, Hennepin County Medical Center, Minneapolis, and the University of Minnesota Medical School, Minneapolis, Minnesota.

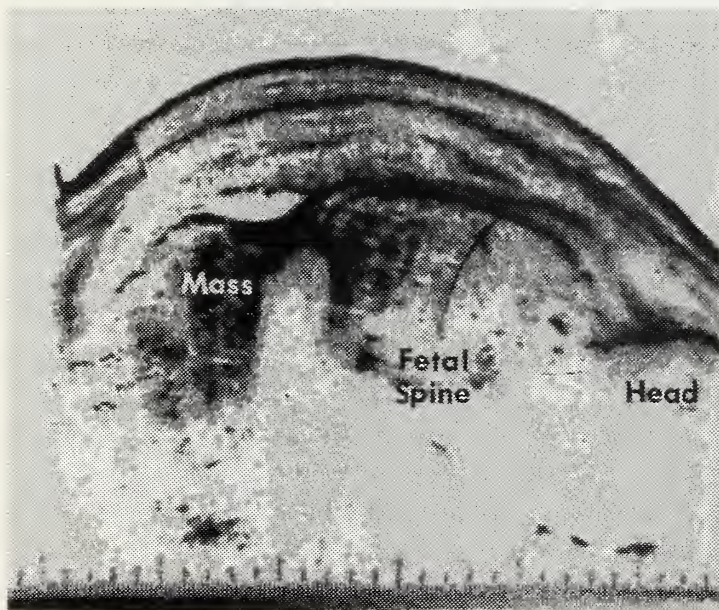


Fig. 1 — Sonogram through the longitudinal axis of the fetus demonstrating fetal head, fetal spine and complex mass arising from caudal pole.

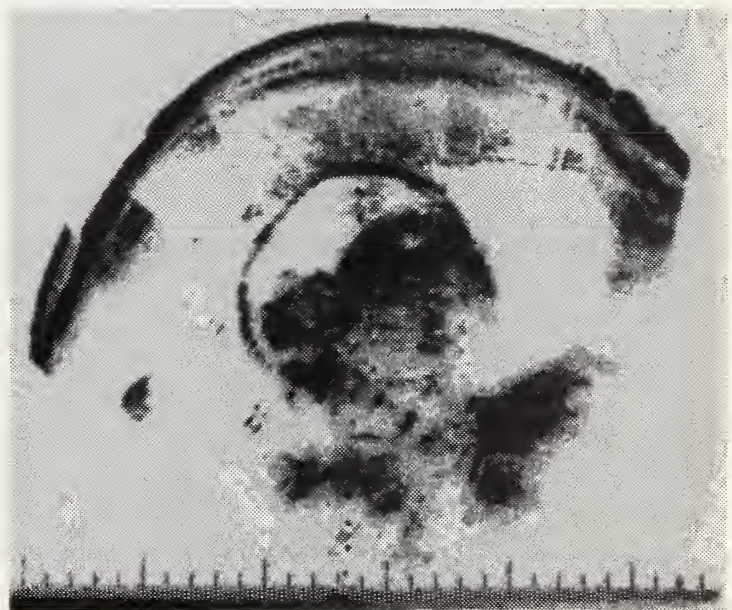


Fig. 2 — Sonogram transversely through the mass showing both cystic and solid areas.



mass, including the coccyx, was performed on the third day of life because the skin overlying the mass was breaking down. The mass weighed 980 grams and contained tissue from all germ cell layers and was without evidence of malignancy. The histologic diagnosis was a benign teratoma. Subsequently, the infant did well and gained weight appropriately. Figure 4 shows the child and the operative site six weeks after birth.

### Discussion

Sacroccocygeal teratomas are relatively rare, but well recognized congenital malformations. They are more common in female infants and are frequently associated with other anomalies. In the neonatal period, the malignancy rate is low, but it increases with time and after four months of life is reported to be 40-50%.<sup>1</sup> Early complete surgical excision of the mass along with the coccyx is stressed by the pediatric surgeons.<sup>1,2</sup> Of more immediate importance is delivery trauma and an apparent tendency in the newborn period for internal hemorrhage with subsequent death of the neonate.

A previous report presented a case associated with acetazolamide.<sup>3</sup> In this case, the patient received no known teratogen but did receive several drugs in early pregnancy.

In a review of the recent literature, we found several cases of sacroccocygeal teratomas diagnosed by ultrasound,<sup>4,5,6</sup> but this information was not used to manage the pregnancy except in one case just recently reported by Horger and McCarter.<sup>7</sup> They had a case very similar to ours in which the prenatal diagnosis of sacroccocygeal teratoma was made and cesarean section was done when labor began.

In summary, we have reported a case in which a presumptive diagnosis of sacroccocygeal teratoma was made prenatally on the basis of the ultrasound studies. Because of the possibility of internal hemorrhage and/or dystocia, abdominal delivery was accomplished with a resultant excellent outcome.



Fig. 3 — Newborn in isolette showing typical appearance of sacroccocygeal teratoma.



Fig. 4 — Baby at six weeks showing operative site with excellent restoration of normal perineal anatomy.

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# Case Report

## Bilateral Renal Cortical Necrosis Report of a Case with Recovery

DONALD M. LARSON, M.D.\* and ROBERT E. WAHMAN, M.D.†

Only rarely do patients with renal cortical necrosis recover from their illness. Finding glomerular thrombi in the renal biopsy usually indicates diffuse cortical necrosis, and recovery is rare. We report a patient who developed cortical necrosis following influenzal pneumonia. Though the kidney biopsy specimen contained numerous glomerular thrombi, the patient recovered, and is well three years later.

**A**BRUPT ANURIA USUALLY indicates serious renal disease which was often fatal before the availability of dialysis. Anuria, caused by diffuse bilateral renal cortical necrosis, results in total loss of kidney function and is always fatal without dialysis. Survival in this disease, with some preservation of kidney function, occurs rarely,<sup>1,2</sup> and indicates partial or incomplete necrosis of the kidney cortex.

Cortical necrosis accompanied by glomerular and arteriolar thrombi is usually diffuse and nearly always fatal. In a review of 38 patients, none of the patients

with glomerular thrombi survived over twenty months.<sup>1</sup>

We are aware of only two patients with cortical necrosis and glomerular thrombi who survived.<sup>2,3</sup>

We are reporting a third patient with glomerular thrombi who survived this usually catastrophic illness.

### Case Report

A sixty-nine-year-old man had a bout of "flu" three weeks before he was admitted to the hospital. During the illness he had a temperature of 102°F (38.9°C), shortness of breath, chest pain, and a productive cough with bloody sputum. After a few days he improved. Symptoms then recurred and persisted. Increasing shortness of breath resulted in admission to another hospital. His chest Xray showed bilateral pneumonia. Tetracyclin and cephalothin were administered initially, but forty-eight hours later were discontinued when total anuria developed. The patient was then transferred to the care of one of the authors (REW).

Pertinent past history included a right lumbar sympathectomy for

\*Associate Professor, Department of Pathology University of Minnesota, Duluth, School of Medicine, Duluth, Minnesota.

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Address Reprints to: Donald M. Larson, M.D., Associate Professor, Department of Pathology, University of Minnesota, Duluth, School of Medicine, Duluth, Minnesota 55812.



Figure — ( $\times 200$ ) Chromotrope Silver Stains. The glomerular capillaries are filled with fibrin thrombi and the arteriole is occluded with a fibrin thrombus. A small artery on the middle right side of the field is also filled with a fibrin thrombus. The tubules contain cellular debris.



arterial insufficiency in the right leg; he later had aortoiliac bypass surgery on the right. He had no further symptoms of claudication, and had no personal or family history of diabetes.

Physical examination revealed an elderly man with dusky skin and rapid, labored breathing. Pulse was 92/minute and blood pressure was 138/80. The lungs contained coarse rales in the right base posteriorly and in the left chest laterally. The right groin contained a well-healed scar. Each femoral artery pulsation was palpable, but the only palpable pulsation in the legs was in the left popliteal fossa.

The admission laboratory studies were: hemoglobin, 16.1 gm/dl; white blood cell count 17,000, with 81% segmented neutrophils and 9% nonsegmented neutrophils; arterial pH, 7.41; partial pressure of carbon dioxide ( $\text{PaCO}_2$ ), 33 mm Hg; bicarbonate, 21 mEq/L; partial pressure of oxygen ( $\text{PaO}_2$ ), 30 mm Hg; blood urea nitrogen, 57 mg/dl; creatinine, 3.8 mg/dl; and plasma glucose, 140 mg/dl. The peripheral blood smear showed increased polychromasia, one nucleated red blood cell per 100 white cells, and adequate platelets. No urine was available for examination.

After the patient had received nasal oxygen (5L of 100%  $\text{O}_2$ /min) for three hours, the partial pressure of oxygen had risen only slightly, to 43 mm Hg.

A diffuse bilateral pulmonary infiltrate seen on chest Xray was interpreted as pneumonia. Cytoscopic examination revealed a normal lower urinary tract; a retrograde pyelogram showed a normal kidney collecting system and normal kidney size.

By the second day his hemoglobin had fallen to 13.5 gm/dl; the white blood cell count had risen to 25,500, with 74% segmented neutrophils and 20% nonsegmented neutrophils. The peripheral blood smear again showed increased polychromasia, two nucleated red blood cells per 100 white cells, with anisocytosis, poikilocytosis and schizocytes. Platelets were adequate. The following additional pertinent laboratory studies were obtained: blood urea nitrogen, 160 mg/dl; creatinine, 6.3 mg/dl; potassium, 5.1 mEq/L; lactic dehydrogenase, 3000 mU/Ml (normal to 200 mU/ml); aspartate aminotransferase, 450 mU/ml (normal to 50 mU/ml). The patient was still receiving nasal oxygen (5L 100%  $\text{O}_2$ /min and the partial pressure of oxygen ( $\text{PaO}_2$ ) had risen to 67 mm Hg.

Later that day the hemoglobin was 11.7 gm/dl, the white blood cell count 27,706, with 46% segmented neutrophils, 46% nonsegmented neutrophils and 2% neutrophilic myelocytes. The peripheral blood smear showed persistent polychromasia, anisocytosis, poikilocytosis, numerous fragmented red blood cells, decreased platelets and three nucleated red blood cells per 100 white cells. The fluorescent antinuclear antibody test was negative and serum complement was normal. The sputum gram stain showed only a few gram-negative rods and a rare neutrophile; cultures later grew out *Pseudomonas* species and *Escherichia coli*. Three separate blood cultures obtained over the first two days were later reported to show "no growth."

Hemodialysis was started on the third day of anuria and repeated every other day. Nasal oxygen was continued, since the patient's breathing difficulties persisted. He was disoriented and delusional. On the sixth day plasma fibrinogen was 300 mg/dl, prothrombin time was normal, and fibrin split products were  $> 10 > 40$ . On the twelfth day, when his breathing had improved, biopsy specimens of kidney tissue and of muscle tissue were obtained. On the same day influenza A titre was 1:1024 (he had received no vaccine).

The following day the patient passed 75 ml of urine, and each successive day he excreted more urine, the volume reaching 1200 ml twenty-three days after the onset of anuria. He received his last dialysis treatment on the twenty-third day and was discharged from

the hospital on the thirtieth day; serum creatinine was 3.1 mg/dl. At the time of discharge the lungs showed improvement on Xray, but the bilateral lung infiltrate persisted.

One month later the lung fields appeared normal on Xray examination.

Nine months later the patient felt well, and had just returned from a hunting trip. Serum creatinine was 1.9 mg/dl. The influenza A titre had fallen to 1:128. Each kidney appeared small on Xray, but no renal calcification was detectable with tomography.

He has continued to be in good health to the present, thirty-six months after the anuric episode.

## Pathology

The kidney tissue contained several congested, but still viable glomeruli just beneath the capsule. The subcapsular tubules showed cellular necrosis and were filled with blood. The remainder of the cortex was completely necrotic. Glomerular capillaries could be seen easily with chromotrope stains. Numerous fibrin thrombi occluded glomerular capillaries and arterioles (Figure). Necrosis of the cortex extended to the corticomedullary junction and, here, there was a sharply-defined transition to viable, intact medullary tissue. The muscle biopsy specimen showed normal histology.

## Discussion

Renal cortical necrosis rarely follows viral infections. Cortical necrosis usually is seen with pregnancy, or its complications — toxemia or premature placental separation, and also accompanies a variety of unrelated conditions, including burns, shock, snakebite, poisoning and bacterial infections.<sup>4</sup> In our patient cortical necrosis followed a bout of influenzal pneumonia.

Another patient who survived cortical necrosis following influenza<sup>3</sup> had disseminated intravascular coagulation, and numerous glomerular thrombi. In our patient a number of laboratory findings suggested that intravascular coagulation may have contributed to the formation of glomerular thrombi.

Numerous glomerular thrombi are commonly seen in diffuse cortical necrosis, and their presence usually indicates irreversible widespread kidney damage.

Our patient demonstrates the limitations of the kidney biopsy specimen findings in predicting the extent of damage. Although the specimen established the presence of a disease which usually is fatal; the patient has recovered sufficient renal function to survive, well and free of dialysis, for three years.

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# Letters to the Editor

Dear Editors:

## **“And the Beat Goes On”!**

The commercial states a well accepted truism. In this case witness the number of recent articles appearing in MINNESOTA MEDICINE and other medical journals concerning H.M.O.s. Sometimes a prejudicial reader, such as myself, wonders if the letters stand for “How Many Opponents”!? It seems that everybody has their opinions pro and con, hopefully based on data rather than emotion. For those of us who happen to be believers it is encouraging to note that many physicians, hospitals, and businesses have changed their convictions during the last two years.

A few observations seem valid at the present time. i.e., purchasers of health insurance, be it families or corporations, are extremely attracted to the prepaid, generally inclusive, H.M.O. concept. Witness the extent of enrollment in many large firms. In addition, even in places like conservative communities as Hartford, Connecticut, the dominant hospital will likely establish an H.M.O. for a variety of reasons. In other areas of the country, not only large hospitals are launching programs but insurance companies, industry, and yes, even many medical societies are both leading and reacting to societal and economic pressures. Hardly a week goes by that I do not receive a long distance phone call from an individual who wants to know all the things there are to know concerning an H.M.O. in ten minutes.

Nine of the fifteen H.M.O.s that began in 1979 were of the I.P.A. type. Six federally sponsored H.M.O.s were closed because of financial difficulty last year also. Is this because of a contagious attitude that when “Uncle Sam” is writing the checks, no one needs to be financially responsible?

The oft heard charge that H.M.O.s enroll the healthier individuals, leaving the medically troubled to existing indemnity plans does not seem to be true. If more coverage can be achieved with less total cost by the use of basic good sense — why not?

H.M.O. participation allows physicians to demonstrate (through advertising) that they are concerned about health care costs. It is hoped that this advertising will stay within the realm of professionalism and ethical propriety.

In some areas of the country (ex Marin County, California) private practice may be squeezed out of existence by H.M.O.s; an unfortunate demonstration of the ‘too little too late’ or ‘it can’t happen here’ philosophy.

H.M.O.s need not be the first step to medical socialism. In fact, whether it be the group, staff, or I.P.A. type, they demonstrate that physicians working together can effectively shape tomorrow’s health care for the benefit and betterment of all.

**Richard K. Simmons, M.D.**  
Medical Director  
Physicians Health Plan

Dear Editors:

## **Rheumatology Corner**

Please run a correction on an error in our article for *Rheumatology Corner* entitled, “Arthritis and Diabetes”, July 1980 issue.\*

In the paragraph regarding “Bronze Diabetes”, we have mislabeled the joints of the hands. Rather than PIP joints (proximal interphalangeal joints) it should be MCP joints (metacarpal joints) of the hands.

**Roger S. Colton, M.D.**  
St. Paul, Minnesota

\*Page 543.



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# Minoxidil

## A Potent New Antihypertensive Agent

RICHARD M. SWEET, M.D.\* and MORRIS DAVIDMAN, M.D.†

Therapy with Minoxidil was initiated in 11 hypertensive patients at Metropolitan Medical Center and Hennepin County Medical Center. Satisfactory improvement in blood pressure was obtained in all eight patients who remained in the study. Three patients did not finish the study for reasons unrelated to the Minoxidil. Concomitant therapy with beta blockers and diuretics was needed to control tachycardia and weight gain. Excessive hair growth was the most common side effect.

**M**INOXIDIL IS A POTENT, peripheral vasodilator, which has been in use in Europe for several years and is now available for general use in the United States<sup>2,6,7</sup>.

It is an extremely potent vasodilator with a direct, relaxant effect on vascular smooth muscle.

In this report, we describe our experience with Minoxidil in patients who had severe hypertension which was not controlled by significant doses of other conventional antihypertensive medications. Our ex-

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**TABLE 1**  
**Summary of Medical Histories and Laboratory Data**

Patient Age	Race	Sex	Past Medical History	Target* Organ Damage	Serum Creatinine Before Minoxidil (mg/dl)	Serum Creatinine After Minoxidil (mg/dl)
56	W	M	Essential hypertension	Grade II retino-pathy	2.3	2.1
60	W	M	Hypertension, 5 years duration	Grade I Fundi	1.6	1.5
45	W	M	Essential Hypertension	LVH. Grade III retino-pathy	3.0	3.3
58	W	M	Diabetes mellitus	Grade II retino-pathy	0.8	1.0
45	N	F	Malignant hypertension, 1977. Optic atrophy secondary to hypertension.	Grade II retino-pathy. LVH	2.1	2.0
32	N	M	Chronic pyelonephritis and obstructive uro-pathy	CHF. Grade II retino-pathy	2.9	2.6
		M	Arteriosclerotic heart disease	LVH		
50	W	M	Hypertension of 9 years duration. CHF. Renal artery surgery 1978.	LVH. Grade II retino-pathy	1.3	1.2
28	W	M	Dialysis. Systemic lupus erythematosus	LVH. Grade II	On dialysis	On dialysis
41	W	M	Arteriosclerotic heart disease	Grade I	1.0	1.0
64	W	M	Renal vascular hypertension	Grade II Retinopathy, peripheral cerebral disease	1.9	2.0

\* LVH — left ventricular hypertrophy  
CHF — congestive heart failure



perience suggests that Minoxidil in combination with diuretics and a beta-blocking agent offers an alternative to the medical treatment of resistant hypertension regardless of existing renal function.

### Patients and Methods

Patients were selected from a population evaluated at Metropolitan Medical Center and Hennepin County Medical Center and their evaluation was supervised by the authors.

Indications for initiation of Minoxidil therapy were as follows: (1) Less than optimal control on other conventional antihypertensive medications at high doses, and (2) Side effects of these drugs when increased to high doses.

Summaries of pertinent medical histories, renal function, and various therapeutic regimens at the time of initiation of Minoxidil are presented in the tables.

### Results

Individual results for changes in systolic, diastolic and mean blood pressures can be found in Tables 3, 4, and 5. Although data is reported at four and twelve weeks, blood pressure reduction was fairly rapid in most patients. Loss of blood pressure control while on Minoxidil therapy was generally associated with either poor compliance or excessive weight gain. There were no complaints of orthostatic hypotension.

By twelve weeks in our patient group there was a significant decrease in mean blood pressure. This amounted to 40 mmHg in the supine position and 22 mmHg in the upright position. The fall in mean blood pressure could be accounted for by significant reduction in both systolic and diastolic blood pressures. In addition to the substantial fall in blood pressures in both positions, patients who previously demonstrated postural hypotension prior to initiation of Minoxidil therapy failed to demonstrate this phenomenon after treatment as seen in five patients.

As shown in Table 5, eight of the original 11 patients remained on therapy for twelve weeks. One patient was placed on chronic hemodialysis, and therapy with Minoxidil was discontinued. Another patient was transferred to another institution, and one patient achieved blood pressure control after a left nephrectomy for renovascular hypertension. Two of these three patients were well controlled on Minoxidil therapy at four weeks.

No patient discontinued Minoxidil because of complications or adverse reactions. Excessive hair growth was common in all patients. Excessive weight gain exacerbating angina pectoris and congestive heart

failure was seen in one patient. This was controlled by additional diuretic therapy.

### Comments

Minoxidil has proved to be a very potent antihypertensive agent. It has had extensive clinical usage in Europe and in clinical studies in this country<sup>1,4</sup>.

TABLE 2

Patient Weight (KG)	Weight, Blood Pressure and Drug Therapy Before Minoxidil Therapy		Blood Pressure <sup>2</sup>	
	Previous Drugs <sup>1</sup>	Total Dosage	Standing	Supine
67.7	P	240 MGM	135/90	210/110
	PR	9 MGM	(105)	(143)
	F	120 MGM		
73.2	P	80 MGM	180/120	198/122
	C	0.4 MGM	(140)	(147)
	F	80 MGM		
74	A	500 MGM	190/112	180/110
	P	400 MGM	(138)	(133)
	H	300 MGM		
	F	160 MGM		
85.5	P	80 MGM	110/80	200/120
	H	300 MGM	(90)	(147)
	C	2.4 MGM		
	F	120 MGM		
89.1	A	1500 MGM	170/122	164/118
	F	240 MGM	(138)	(133)
	P	360 MGM		
	H	50 MGM		
	G	20 MGM		
86.9	A	1000 MGM	130/80	180/110
	PR	8 MGM	(97)	(133)
	H	200 MGM		
	F	160 MGM		
111.4	C	0.2 MGM	168/110	184/118
	F	80 MGM	(129)	(140)
	H	300 MGM		
	P	300 MGM		
74.1	C	2.4 MGM	94/50	192/102
	HZCT	100 MGM	(65)	(132)
	F	40 MGM		
	PR	20 MGM		
84.1	P	160 MGM	160/110	200/110
	PR	16 MGM	(127)	(140)
	F	80 MGM		
69	P	480 MGM	(---) <sup>3</sup>	170/110
	PR	20 MGM	(---)	(130)
101.8	P	960 MGM	140/110	144/110
	F	160 MGM	(120)	(121)
	S	100 MGM		
	PR	18 MGM		

<sup>1</sup>M Minoxidil

P Propranolol

F Furosemide

Pr Prazosin

H Hydralazine

A  $\alpha$ -methyl dopa

C Clonidine

HCTZ Hydrochlorothiazide

S Spiranolactone

G Guanethidine

M Metolazone

<sup>2</sup>Mean blood pressure, in brackets, is estimated as 1/3 the pulse pressure plus the diastolic pressure.

<sup>3</sup>Not obtained



Pharmacologic studies have indicated that Minoxidil, a piperidino-pyrimidine derivative, has a direct relaxant effect on vascular smooth muscle and has no inherent effect on adrenergic function. Consequently, blood pressure reduction results from a selective relaxation of peripheral smooth muscle.

Minoxidil may be given without regard to renal function, its use being indicated as an alternative therapy to nephrectomy in severe hypertension associated with end stage renal disease and in patients undergoing chronic hemodialysis therapy<sup>11</sup>.

Minoxidil efficacy in the treatment of severe hypertension has been shown in a number of clinical trials. Minoxidil can be given fairly rapidly, in increasing increments up to a maximum dose of 80 mg per day in a stepwise fashion<sup>8,9</sup>. Beta-blockade is essential before initiation of Minoxidil because of the significant reflex tachycardia that is associated with the intense vasodilatation produced by Minoxidil. Because of this phenomenon patients with an unstable cardiovascular status should be followed closely while initiating Minoxidil. Angina pectoris has been reported

to be precipitated in patients without adequate beta-blockade. T wave abnormalities, including T wave inversions, have been noted after initiation of Minoxidil therapy. However, these changes are not indications to discontinue therapy as no adverse cardiac effects have been associated with these changes. Fluid retention on Minoxidil can be dramatic, and it is necessary to have the patient on adequate amounts of diuretics at the initiation of Minoxidil therapy. Our experience and that of others suggests that Loop diuretics are the diuretics of choice. Occasionally it may be necessary to add metolazone to the therapeutic regimen to further enhance the renal excretion of excess sodium and water brought about by reflex renin release. Generally, it is best to initiate Minoxidil therapy with a dosage of 5 mgm orally, followed within six to twelve hours by a dosage of equivalent amount. Various dosing schedules have been proposed for Minoxidil. However, doubling the dosage every twenty-four hours enables rapid control of hypertension. For example, one could start with 5 mgm in the morning and an additional 2.5 to 5 mgm

TABLE 3

**Weight, Blood Pressure and Drug Therapy Four Weeks after Minoxidil Therapy**

Patient Weight (KG)	Previous Drugs		Blood Pressure		Change in Mean Blood Pressure	
	Total	Dosage	Standing	Supine	Standing	Supine
68.2	M —	40 MGM	130/70	134/74		
	P —	240 MGM	(90)	(94)	(-15)	(-49)
	F —	160 MGM				
75	M —	40 MGM				
	P —	360 MGM	160/92 (115)	150/94 (113)	(-25)	(-34)
72.7	M —	30 MGM	110/70	120/70	(-55)	(-46)
	P —	360 MGM	(83)	(87)		
	F —	120 MGM				
91.4	M —	40 MGM	152/98	152/106	(+26)	(-26)
	P —	400 MGM	(116)	(121)		
	H —	200 MGM				
	F —	240 MGM				
90.5	M —	70 MGM	150/94	158/94	(-25)	(-18)
	P —	420 MGM	(113)	(115)		
	F —	440 MGM				
82.9	M —	30 MGM	126/84	122/74	(+1 )	(-43)
	P —	240 MGM				
	F —	80 MGM				
117.3	M —	40 MGM	142/100	162/92	(-15)	(-24)
	P —	360 MGM	(114)	(116)		
	F —	120 MGM				
85.4	M —	25 MGM	132/90	128/80		
	P —	240 MGM	(104)	(96)	(-23)	(-44)
	F —	80 MGM				
69	M —	15 MGM	114/80	132/80	(--)	(-36)
	P —	120 MGM	(91)	(94)		
99.1	M —	40 MGM	114/90	118/80	(-22)	(-28)
	P —	1120 MGM	(98)	(93)		
	F —	480 MGM				
	S —	200 MGM				

<sup>1</sup> Not done



again in the evening. The second morning dose could then be 10 to 15 mgm, while the second evening dose could be 7.5 to 10 mgm. By the third day the patient could receive 20 mgm in the morning and 10 mgm in the evening for a total of 30 mgm daily which is an average dose in an adult. The maximum recommended dosage in adults is 100 mgm daily<sup>13</sup>. Minoxidil has been used successfully to treat hypertension in the pediatric age group<sup>3,5</sup>. Initial and maintenance doses are smaller. A similar need for beta-blockade and diuretic therapy is seen in this age group.

The drug half-life of Minoxidil may be as short as four hours. The pharmacologic half is prolonged up to 24 hours in hypertension. This enables one to give the drug once or twice daily.

Excessive hair growth is the most troublesome side effect of Minoxidil. It is seen in approximately 70% of

patients taking the drug. Side effects other than edema, tachycardia and angina have been minimal.<sup>13</sup>

Adverse hemodynamic effects on the pulmonary circulation are not encountered with Minoxidil and the reflex tachycardia is generally easily controllable<sup>10,12</sup>. Cases of right atrial necrotic lesions have been reported in animals receiving Minoxidil. However, this has not been seen in humans<sup>13</sup>.

### Summary

Minoxidil is an extremely potent vasodilator that is indicated in the treatment of severe hypertension when other conventional drugs are ineffective. Concomitant therapy with diuretics and beta-blocking agents is mandatory.

### Acknowledgments

The authors wish to thank Nancy Westburg Johnson and Bridget Stellmacher for their help in preparing this manuscript.

TABLE 4

#### Weight, Blood Pressure and Drug Therapy Twelve Weeks after Minoxidil Therapy

Patient Weight (KG)	Present Drugs		Blood Pressure		Change in Mean Blood Pressure	
	Total Dosage		Standing	Supine	Standing	Supine
70.0	M —	50 MGM	130/70	152/70	(-15)	(-46)
	P —	320 MGM	(90)	(97)		
	F —	160 MGM				
	Z —	5 MGM				
78.2	M —	40 MGM	142/88	126/80	(-34)	(-52)
	P —	360 MGM	(106)	(95)		
	F —	160 MGM				
73.2	M —	25 MGM	108/68	128/84	(-57)	(-38)
	P —	360 MGM	(81)	(95)		
	F —	120 MGM				
92.7	M —	40 MGM	138/96	130/86	(+20)	(-48)
	P —	360 MGM	(110)	(99)		
	F —	620 MGM				
87	M —	80 MGM	130/78	134/84	(-43)	(-32)
	F —	300 MGM	(95)	(101)		
	M —	15 MGM				
	P —	420 MGM				
86.4	M —	30 MGM	128/80	130/82	(-1)	(-35)
	P —	240 MGM	(96)	(98)		
	F —	80 MGM				
105.5	M —	40 MGM	130/84	134/84	(-30)	(-39)
	P —	360 MGM	(99)	(101)		
	F —	240 MGM				
106.8	M —	40 MGM	120/100	110/80	(-13)	(-31)
	P —	960 MGM	(107)	(90)		
	F —	480 MGM				
	S —	200 MGM				

TABLE 5

#### Changes in Supine and Upright Mean Blood Pressure (MBP), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) Before and During Minoxidil Therapy\*

	MBP		SBP		DBP	
	Supine	Upright	Supine	Upright	Supine	Upright
Before	137 ± 3.1	120 ± 7.1	183 ± 7.5	153 ± 9.9	115 ± 1.9	103 ± 6.1
4 Weeks	104 ± 4.9	103 ± 4.5	140 ± 6.4	136 ± 6.5	86 ± 4.5	87 ± 4.1
P	< .001	(.09)	.001	(.19)	< .001	.05
12 Weeks	97 ± 1.3	98 ± 3.4	131 ± 4.1	128 ± 3.7	81 ± 1.8	83 ± 4.0
P	< .001	.04	< .001	(.07)	< .001	.03

\* All data expressed as mean standard error of the mean.



# Review

## Role of Transfemoral Lumbar Epidural Venography in the Diagnosis of Herniated Lumbar Discs

SIDNEY K. SHAPIRO, M.D. PH.D.;\* S. M. TADAVARTHY, M.D.,† and S. GORDON, M.D.†

Lumbar epidural venography was performed in forty patients. In twenty-one patients the venogram was positive for the radiological diagnosis of herniated lumbar disc. The results of venography were correlated with either myelography or discography or with both in twenty-nine patients. Only by the use of a combination of these procedures can we hope to arrive at a desirable level of diagnostic accuracy.

SINCE 1968 TRANSFEMORAL ascending lumbar catheterization of the epidural veins popularized by Gargano et al.<sup>1</sup> and LePage<sup>2</sup> has largely replaced other techniques for visualization of the epidural veins. This procedure (transfemoral ascending lumbar catheter (TACL) epidural venography) according to scattered reports has yielded excellent results in the diagnosis of lumbar disc disease. This technique has as yet not been widely adopted and its value has not been fully appreciated by the medical profession. It is the purpose of this communication to review our experience with this procedure and to underline its usefulness and limitations in the diagnosis of ruptured lumbar discs.

### Radiological Anatomy

The lumbar venous system, which is valveless, has two basic components: one set of veins runs inside (internal vertebral veins) and the other outside (external vertebral veins) the vertebral canal. These longitudinal vessels anastomose through transverse channels and are connected with the inferior caval system. These two systems run parallel and have connecting veins.

#### *Internal Vertebral Veins*

Inside the vertebral canal, there are two groups of veins that run longitudinally. One lies on the posterior surface of the vertebral bodies and the other just anterior to the dorsal wall of the vertebral canal. The latter, posterior internal vertebral veins, are generally considered of little significance. The left and right anterior internal vertebral veins (AIVV) however are of cardinal importance being closely applied to the posterior surface of the vertebral bodies and the intervertebral discs. These veins present a wavy pattern in the anteroposterior projection, curving

laterally at the level of the disc and medially at the level of the pedicles, where there is usually a cross connection between both sides by transverse venous channels. At the sacral level, lateral sacral veins



Fig 1 — The catheter is selectively placed in the left ascending lumbar vein as pointed by the curved arrow. The numbers from 1 through 6 represent the hexagon. The struts 2, 3, 5, 6 represent the left and right anterior internal vertebral veins on either side of spinal canal. The numbers 1 and 4 represent the transverse channels that connect the anterior internal vertebral veins on either side and complete the so called "hexagon". The straight arrows represent the supra and infra intervertebral veins.

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connect the vessels within the vertebral canal with the internal iliac vein via the anterior sacral foramina. J. T. Wilmink et al.,<sup>3</sup> who detailed the radiological anatomy, point out that for daily clinical use the term "anterior internal vertebral veins" is cumbersome and they prefer the term "epidural veins" which is now commonly used.

The right and left anterior internal vertebral veins with their transverse connecting venous channels basically simulate a "stack of hexagons". The struts of this six-sided structure (Figure 1) are interrupted when there is disc bulging or herniation (Figures 2 and 3).

#### *External Vertebral Veins*

They are located outside the vertebral canal and are divided into anterior and posterior external vertebral venous plexus. The posterior external vertebral venous plexus is located posterior to the transverse processes, vertebral arches and spinous processes. The ascending

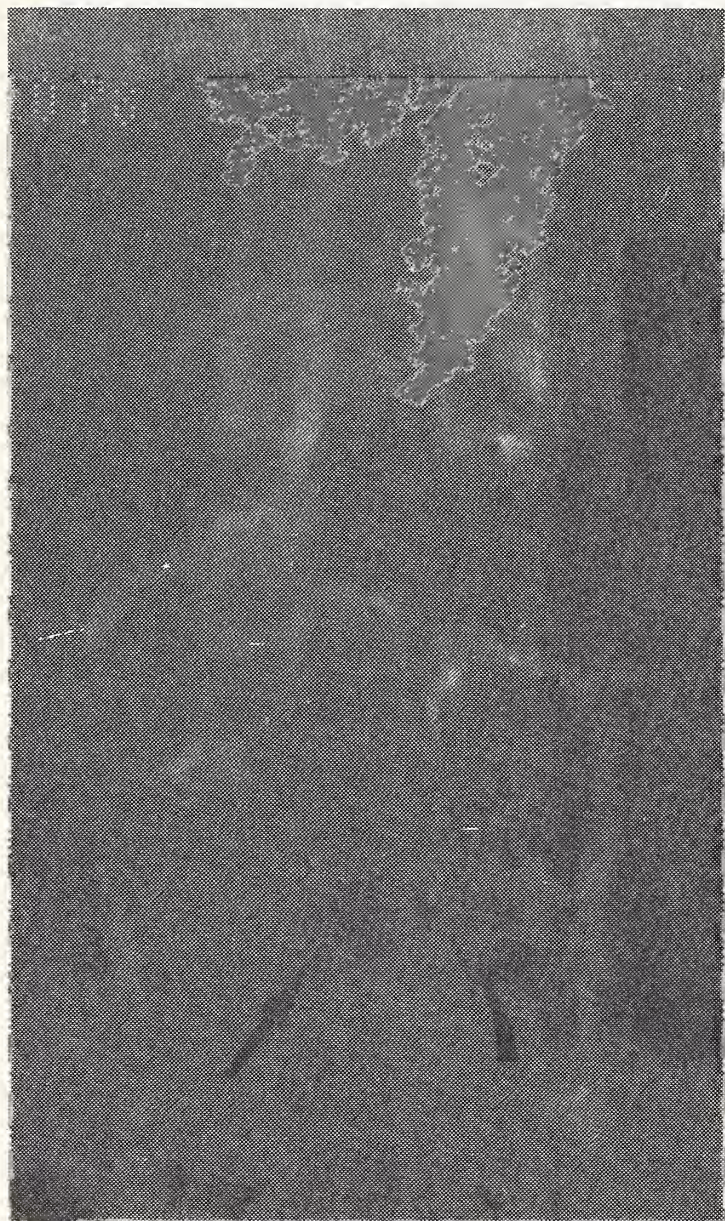


Fig. 2 — There is complete interruption of right anterior internal vertebral vein secondary to herniated disc (straight arrow). The left anterior internal vertebral vein (curved arrow) is in normal position and shape.



Fig. 3 — The straight arrow points to the lateral displacement and marked thinning of right anterior internal vertebral vein secondary to herniated disc. The curved arrow on the contralateral side represents the normal configuration of left anterior internal vertebral vein.

lumbar veins are the important components of the anterior venous plexus and run in the paravertebral gutters on either side. These veins (ALV) usually arise from the common iliac vein on either side and finally drain into the azygous and hemiazygous veins.

The intervertebral veins (otherwise known as the supra and infra-pedicular veins) connect the internal vertebral veins inside the spinal canal to the ascending lumbar veins that run in the paravertebral gutters on either side. Two intervertebral veins (IVV) usually pass through each intervertebral foramen, roughly parallel to the emerging nerve root, one above and one below each pedicle. There may be some variations in the venous anatomy but in any one patient, there is a side to side asymmetry and a level to level similarity. On occasion, the ascending lumbar veins may be rudimentary and difficult or impossible to catheterize. The rationale of epidural venography rests upon the anatomical fact that the anterior internal vertebral veins bear a constant relationship to the vertebral bodies and hence to the intervertebral discs.

Venographic findings of lumbar disc herniation (see Figures 2 and 3) are produced when the herniated disc gradually compresses, thins, displaces and finally obstructs the adjacent veins. Gargano et al.<sup>1</sup> have listed



the most important signs: (1) abnormal curvature of an anterior internal vertebral vein. The vein is usually bowed laterally on the anteroposterior view of the venogram being displaced posterolaterally by the herniated disc. However, the direction of the displacement varies and may be medial depending upon the direction of the disc herniation. (2) Unilateral or bilateral occlusion of the anterior internal vertebral vein as it crosses the disc interspace. Sometimes complete block of both anterior internal vertebral veins will prevent filling of the epidural plexus above the level of the herniation. Supplementary findings which are in themselves nondiagnostic but which may be significant are suprapedicular vein occlusion, localized dilatation of the epidural and extravertebral veins and opening of collateral channels around the obstructed veins.

### Technique

Both groins are prepared for femoral vein punctures. Although catheterization of the ascending lumbar vein on the symptomatic side has been recommended, it is easier to catheterize the left ascending lumbar veins since it has a constant relationship to the left iliac vein. The relationship of the right ascending lumbar vein to the right iliac vein is less constant. There are no valves in the epidural veins and therefore good cross filling generally occurs. Routinely salts of meglumine iodide contrast material were used. This contrast material minimizes the pain at the time of venography. Coincident with the injection of the contrast material, a deep Valsalva maneuver (forced expiration against the closed glottis) to increase the inferior vena cava pressure is carried out. Some investigators prefer the use of external abdominal compression but in our experience this is required only infrequently. Following catheterization of the left ascending lumbar vein, an attempt is made to selectively catheterize the intervertebral vein (the supra and infra-pedicular veins). If this can be accomplished, excellent visualization of the L5-S1 disc level can usually be accomplished and a small quantity of contrast material used. If satisfactory visualization of the epidural veins is not obtained with the first injection, bilateral injections are carried out with two catheters in place with either both ascending lumbar veins being injected or the left ascending lumbar vein and the right lateral sacral veins being injected simultaneously. If the L5-S1 disc level has not been well visualized the right and left sacral veins are injected simultaneously.

The rate of contrast material injection depends upon the number of catheters to be injected and the site of

catheter placement. When a unilateral injection was performed, usually 30 cc. of contrast was injected. Bilateral injections were accomplished by injecting 50 cc. of contrast material. The rate of injection is usually 3 to 5 cc. per second if direct catheter placement was achieved in the L5-S1 intervertebral vein. If simultaneous injections of a lateral sacral and the ascending lumbar vein are performed, the rate of injection is 8 to 10 cc. per second. Depending upon the flow rate and the site of injection films were obtained at a rate of one per second for 10 to 15 seconds. Routinely subtraction and magnification venography was done on each case. The procedure was completed within 20 to 40 minutes depending upon the number of injections required. Sometimes the ascending lumbar veins on one or both sides are rudimentary and are formed by multiple venous channels. In the latter situation it is virtually impossible to selectively catheterize the ascending lumbar veins. In one patient in this series, rudimentary lumbar veins precluded a satisfactory procedure. In patients who have had previous back surgery with discotomy and laminectomy, the anterior internal vertebral veins are usually occluded at the level of the previous surgery. Accordingly venography has limited value in this group of post-surgical patients. It is important technically to fill all of the veins above the unopacified segments before any decision is made with respect to venous occlusion. Every effort should be made to have the contrast reach the veins at all levels. The epidural veins proximal and distal to the unfilled veins must be well opacified. In some patients with rudimentary ascending lumbar veins, the procedure can be completed by selective injection into the right and left lateral sacral veins.

### Results (See Summary Table 1)

Forty-one consecutive patients on whom epidural venography was performed, constitute the basis of this study. In one patient, rudimentary ascending lumbar veins precluded a satisfactory procedure and this patient will not be considered further. Twenty-five of the patients were male and fifteen of the patients were females. The ages range from twenty to sixty-nine and

TABLE 1

#### Summary — Forty Patients

<b>A. Groups I and II.....</b>	<b>29 patients</b>
Positive Ruptured disc .....	24
Positive Myelograms .....	16
Positive Venograms .....	14
Positive Discograms .....	12
Lack of Correlations	
Between Venogram and Myelogram .	14
<b>B. Group III .....</b>	<b>11 patients</b>
Positive Venograms .....	5



the breakdown of the ages by decades is reflected in Table 2. Eighteen patients (group I) had venography, myelography and discography; eleven patients (group II) had venography and myelography; and eleven patients (group III) had venography alone. Of particular interest are the group I and group II patients who together constitute twenty-nine patients. Of these twenty-nine patients, twenty-four had a positive radiological diagnosis of ruptured intervertebral disc or discs. In this group, there were 16 positive venograms and there were fourteen positive myelograms. There was a lack of correlation between venography and myelography in fourteen patients. Venogram was positive in six patients for ruptured disc at the L5-S1 level. These six patients would have been missed since the myelograms were negative. The venogram was positive at the L4-L5 level in two patients in whom the myelogram was negative. The myelogram was positive at the L4-L5 level in six patients in whom the venogram was negative.

**TABLE 2**  
**Age of Patients**

<u>Age Range</u>	<u>No. of Patients</u>
20-30	11
30-40	10
40-50	13
50-60	3
60-70	4

In the first group of eighteen patients in whom all three procedures were done, three patients with ruptured discs would have been missed if only venography and myelography were performed. In these three the discogram revealed evidence of ruptured discs: In one at the L3-L4 level, in another at both the L3-L4 and the L4-L5 levels; and in the third at the L4-L5 level. In one additional patient there was a frank rupture at a level not demonstrated by myelography. Myelography had indicated a ruptured disc at the L4-L5 level. This was confirmed by discography at the L4-L5 level but there was an additional rupture at the L5-S1 level. In one case the venogram was reported as positive at the L4-L5 level while the myelogram and discogram were entirely normal. This patient in our opinion did not have a ruptured disc and the venogram was a false-positive.

Five additional positive epidural venograms were obtained in group III raising the total number of positive venograms to twenty-one. In this group of eleven patients (group III) concern about myelography caused the patients to refuse this procedure and without venography, further objective information with respect to the status of the disc would not have been possible.

## Discussion

In a clinical setting, short of surgery, an absolute diagnosis of a ruptured lumbar disc is not possible. Such conditions as lateral spinal stenosis, spur formation and anatomical variations may result in false-positives on Xray diagnosis. However, in a high percentage of cases, a presumptive diagnosis of ruptured disc can be made when positive Xray findings are correlated with the clinical picture. A presumptive diagnosis of ruptured lumbar disc allows aggressive medical treatment to be carried out. In this series, only one patient came to surgery. This patient in group I had surgical confirmation of a ruptured L5-S1 disc. In this patient the myelogram was negative. The epidural venogram and the discogram were positive. The small number of patients going to surgery in this series reflect the current philosophy in this clinic that with aggressive medical treatment, surgery can be avoided in the majority.

Lumbar epidural venography has been reported in the literature as varying in accuracy from 78 to 91 percent<sup>4</sup>. In our series epidural venography did not produce this degree of accuracy with only sixteen positive venograms in the twenty-four patients with a radiological diagnosis of ruptured discs (66%). In group III, in which only venography was performed, five additional patients were found to have radiologic findings of ruptured disc.

On myelography the percentage of diagnostic accuracy varies according to various authors from as low as 67% to as high as 100 percent<sup>5</sup>. Myelography will be diagnostic of posterolateral disc herniation only if the disc impresses the contrast column. There are several situations where there may be nerve root compression without corresponding pressure defects. The nerve root may be caught laterally beyond the reaches of the subarachnoid sac; the dural sac may be attached posteriorly away from the disc so that the disc may not impress it but may still catch the nerve root passing forward toward the intervertebral foramen; or the dural sac may terminate above the lumbosacral level. In our series, myelography proved to be successful in demonstrating a ruptured disc in only fourteen of twenty-four patients (58%).

The role of lumbar discography in the diagnosis of ruptured lumbar disc has been reviewed in the monograph of Collis<sup>6</sup> and more recently by Shapiro<sup>7</sup>. Discography is a limited specialized procedure designed to study the status of lumbar intervertebral discs. Discography has the distinct advantage of providing direct visualization of the intervertebral disc itself. In this study a degenerated disc demonstrated by



discography was considered to be significant only if the myelogram and/or venogram were positive. The diagnosis of a ruptured disc on the basis of discography alone was made only when there was a posterior or posterolateral rent in the annulus with the demonstration of a herniation tract. The importance of discography is underlined by the fact that three cases had ruptured disc with posterolateral herniation in which both the venogram and myelogram were within normal limits and in one additional case, a second space demonstrated a posterolateral herniation when the myelogram had revealed evidence of rupture at only one space. The presence of a normal lumbar discogram rules out a ruptured disc and will avoid unnecessary surgery in the presence of atypical or false-positive findings on venography or myelography. One such patient with a false-positive venogram was present in our series. In this patient, the venogram was positive but both the myelogram and discogram were entirely normal.

In general our experience parallels that of Gershtater et al.<sup>8</sup> who indicate that myelography is more accurate at the L4-L5 level while venography is more accurate at the L5-S1 level. However, it is obvious on analyzing the data that no one radiological procedure can establish the diagnosis of disc herniations. Only by a consideration of all three procedures; namely, venography, myelography and discography can the diagnosis of ruptured disc be established radiologically. Sackett, et al.<sup>9</sup> used discography in their study on epidural venography and this group stressed the unreliability of epidural venography in lumbar disc disease when used as the sole procedure.

Epidural venography is well tolerated by the majority of patients and has a minimum of complica-

tions. The injection is usually associated with mild transient discomfort. In our series, only three complications from epidural venography were encountered — one anaphylactic reaction coincident with the injection of the contrast, one pelvic hematoma and one case of persistent inguinal pain. This patient following epidural venography developed an inguinal hematoma. This resolved uneventfully but was followed by persistent inguinal pain. No anatomical basis for same can be demonstrated. The complications of myelography (postspinal headache and possible late arachnoiditis) are avoided. The patients who have had all three procedures are unanimous in their selection of epidural venography as the least traumatic procedure. Prior to surgery it is essential to perform myelography to eliminate consideration of other extradural lesions such as a tumor. If the myelogram is negative and the epidural venogram is positive, discography will resolve the problem of whether there is a normal disc and avoid unnecessary surgery on false-positive venograms. The criteria for the X-ray diagnosis of positive herniated disc on venography in this series were (1) unilateral or bilateral occlusion of the anterior intervertebral vein as it crossed the disc space and (2) abnormal curvature of an anterior internal vertebral vein. The remainder of the signs proved to be unreliable and did not in this series establish a positive diagnosis.

### Conclusions

Transfemoral lumbar epidural venography provides a valuable additional tool in the radiological diagnosis of lumbar disc herniation when its use and limitations are understood.

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# Minnesota Department of Health

## Newborn Metabolic Screening in Minnesota

### I. Congenital Hypothyroidism

MALCOLM B. JENKINS, Ph.D.\* and MICHAEL H. FOLEY, B.S.†

Newborn hypothyroidism screening of all Minnesota infants has been instituted at the Minnesota Department of Health. The same blood specimen is used for phenylketonuria and galactosemia as well as hypothyroidism screening. Initial results indicate the efficacy of this program.

One of the most important characteristics of a successful newborn screening program is a close working relationship between the screening laboratory and local hospitals and physicians.

OVER THE PAST few years, congenital hypothyroidism has proved to be an important addition to most newborn metabolic screening programs. This condition, one of the more common preventable causes of mental retardation, has an incidence of one in several thousand births. It now is easily detectable biochemically (although rarely suspected clinically) in newborns, and is eminently amenable to early therapy. It is most often caused by thyroid gland maldevelopment, a sporadic occurrence, but may also be recessively inherited as an inborn error of thyroid hormone biosynthesis (dyshormonogenesis). About one case in ten results from pituitary or hypothalamic insufficiency.

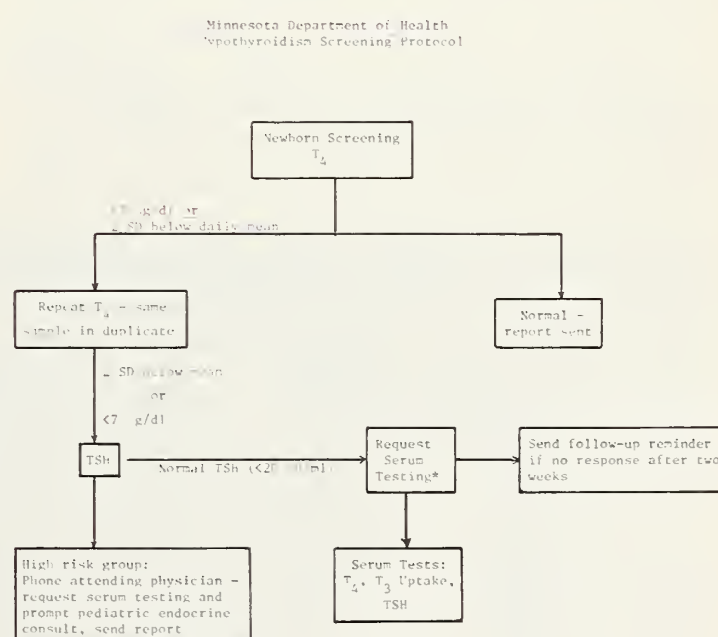
On the recommendation of the Minnesota Department of Health's Ad Hoc Advisory Committee on Newborn Metabolic Screening, the Department began performing hypothyroidism screening on newborn filter paper blood specimens in early 1978. The results of this screening through December of 1979 are reported here. A future report in this series will deal with phenylketonuria and galactosemia screening in Minnesota.

#### Methods

With the adoption of revised Minnesota Department of Health Rule 172 regulating newborn screening in Minnesota, a capillary blood sample from each infant, dried on a standard filter paper specimen card, is required to be sent to the Department for testing within five days after birth. A whole blood thyroxine ( $T_4$ )

determination is made by radioimmunoassay on a single 1/8 inch dot punched by hand from each sample. Commercial reagent kits are used for all radioimmunoassay testing.

The Figure depicts logistics of the Minnesota screening program over the initial year and a half of full scale operation. Approximately the lowest 10% of samples from each  $T_4$  run are repeated the following day in duplicate. Those duplicates determined to be 2 SD below the daily mean or less than 7  $\mu\text{g}/\text{dl}$  (whichever is higher) are selected for thyroid stimulat-



\*MDH requests either a serum sample for testing or the results from such testing if done elsewhere.

\*Human Genetics Unit, Minnesota Department of Health, Minneapolis.

†Division of Medical Laboratories, Minnesota Department of Health, Minneapolis.

Figure



ing hormone (TSH) determination, performed by RIA on the same blood sample. Approximately 2% of all newborns are tested for TSH. If the TSH is elevated, primary hypothyroidism is suspected and the results are reported immediately by phone and letter to the attending physician, with a follow-up call two days later. If the filter paper TSH is not elevated, a serum thyroid function determination is requested by written report. Even when the screening TSH is normal, follow-up testing is indicated on infants with low screening  $T_4$  values in order to identify cases of hypothyroidism secondary to hypothalamic or pituitary deficiency and other rare cases of insufficient thyroid reserve. Serum testing is available through the Minnesota Department of Health. In cases where the screening  $T_4$  is very low (less than  $4 \mu\text{g/dl}$ ; about 0.5% of all samples) and no serum sample or serum test results are received within two weeks of reporting, a reminder is sent to the attending physician. Financial assistance for diagnosis and treatment is available through the Services for Children with Handicaps, Minnesota Department of Health.

### Results and Discussion

Newborn hypothyroidism screening at the Minnesota Department of Health began in January of 1978 with a small pilot program limited to several Twin Cities hospitals. The program was generalized by July of 1978 with the development of larger specimen cards which permitted adequate blood for TSH determination.

Since the institution of hypothyroidism screening at the Minnesota Department of Health, nine cases of congenital hypothyroidism have been detected as of January 1, 1980, an incidence of 1 in 10,000 births. These cases are summarized in the Table. One instance

of presumed secondary hypothyroidism (Case 1) and one case of dyshormonogenesis (Case 3) were among these first nine. All cases of primary hypothyroidism had a grossly elevated screening TSH with the exception of Case 4. Case 4 was not detected in the newborn screen. Her newborn specimen, taken at eight days of age, had a  $T_4$  of  $9.0 \mu\text{g/dl}$  and TSH of less than  $19 \mu\text{U/ml}$ . A second screening specimen at age 20 days gave a  $T_4$  of 0 and TSH of over  $185 \mu\text{U/ml}$ . The newborn sample was positively identified as the infant's by red cell and serum protein polymorphism analysis. The reason for the normal results in this infant's first screening specimen is unclear. It is possible that occasional cases of thyroid dysgenesis will be missed using a 2 SD below-the-mean cutoff<sup>1</sup>, but this case would not have been detected regardless of the cutoff. We are aware of no cases of permanent congenital hypothyroidism missed in other screening programs because of normal  $T_4$  and TSH in the screening specimen, although transient neonatal hypothyroidism of unknown cause has been reported in full term infants<sup>1,2</sup>. Only one infant (Case 4) among those detected in our screen was clinically suspected of being hypothyroid, and signs in that infant were minimal. It must therefore be emphasized that *clinical signs of congenital hypothyroidism are rarely obvious in the newborn*. Indeed, this remains the primary reason for biochemical newborn hypothyroidism screening.

Twenty one cases of presumed thyroxine binding globulin (TBG) deficiency (1 in 4,300 newborns) were found as the result of serum follow-up testing on low  $T_4$  screens. These were determined on the basis of a low  $T_4$ , normal TSH and elevated  $T_3$  resin uptake, and represent a benign, inherited diminished level of thyroxine binding globulin. All but one of these cases

TABLE  
Hypothyroid Cases in Minnesota — January 1978 through December 1979

Case/Sex	Age at Report (days)	Screening Results		Serum Results		Age Therapy Begun (days)
		$T_4$ ( $\mu\text{g/dl}$ )	TSH ( $\mu\text{U/ml}$ )	$T_4$ ( $\mu\text{g/dl}$ )	TSH ( $\mu\text{U/ml}$ )	
1/M*	17	1.5	<20	2.7	3	*
2/F	13	4.2	>175	2.2	596	34
3/M	15	0	>186	<1	1056	27
4/F†				1.9	>250	†
5/F	12	0.5	>183	<1	>250	13
6/M	25	0.7	>183	0.9	"elevated"	31
7/F	15	3.2	>219	1.1	>100	19
8/F	17	3.4	>207	Not performed**		17
9/M	22	7.7	>280	3.8	>100	27
Average:	17			Average:		24

\*This patient was ascertained from repeated filter paper samples. Serum testing, performed locally, was interpreted as "borderline normal". The patient was referred for diagnosis at age 4 months (see text).

†This case was not ascertained on a 3-5 day sample (see text).

\*\*Attending physician regarded screening test as diagnostic



have been males, reflecting the usual X-linked mode of inheritance. We consider TBG deficiency to be a common finding in the population at large, detected only by those screening programs which have a serum follow-up policy. Two cases of apparent TBG excess (manifested only by very low  $T_3$  uptake) have also been ascertained on serum follow-up testing.

One instance of false positive low screening  $T_4$  with elevated TSH was experienced. The newborn filter paper TSH level from this infant was  $>300 \mu\text{U/ml}$  and  $250 \mu\text{U/ml}$  in duplicate assays. Serum testing on this infant at three weeks of age indicated a normal  $T_4$  and a TSH of  $9.2 \mu\text{U/ml}$ . The significance of such apparently spurious screening TSH elevation is unknown at present; similar cases have been found very rarely in other screening programs<sup>3</sup>. The predictive value of a grossly elevated screening TSH with low  $T_4$  is thus 0.9 for our program, based on the first nine cases of hypothyroidism.

The hypothyroidism incidence thus far observed in Minnesota is considerably below the overall reported incidence from the largest North American screening programs of about 1 in 4,200<sup>1</sup>. The detection of secondary hypothyroidism and TBG abnormalities indicates that our protocol and methodology are sensitive. Therefore, although the difference is statistically significant ( $p = 0.05$  determined by chi-square analysis, assuming an incidence of 1 in 5,000), the low incidence may reflect statistical uncertainty and/or geographic variation. The combined incidence from the North Dakota and Wisconsin state screening programs is about 1 in 5,700 (23 cases in around 130,000 births).

The majority of infants with low screening  $T_4$  are premature or have an acute illness. These conditions can depress  $T_4$  values in newborns<sup>4-6</sup>, and this is the largest factor causing "false positive" results. Most such infants are under the care of a neonatologist who is likely to recognize this problem. Repeat testing at several weeks of age is recommended on these infants in order to ensure their euthyroidism.

The Minnesota newborn screening program has been developed along lines endorsed by committees of the American Thyroid Association<sup>7</sup>, American Academy of Pediatrics<sup>8</sup>, and National Academy of Science<sup>9</sup> which uniformly recommend a strong regional laboratory as a cardinal feature of such programs. Centralized screening facilities are recommended because of increased cost effectiveness and improved quality of results. In hypothyroid screening a

large daily sample load is essential in order to generate a statistically valid cutoff value without an excess of false positive results. The average age at institution of treatment in our experience is 24 days. Although this age is well within the guidelines of the American Thyroid Association<sup>7</sup>, we would like to see it still lower. All of the longer delays in starting treatment (Table) resulted from difficulty in getting patients recalled for definitive testing. To this end, close rapport between the Minnesota Department of Health and local physicians and hospitals is necessary to facilitate early diagnosis and treatment. This especially includes prompt attention to mailing in specimens, reporting results promptly from the Department laboratory, and prompt action by attending physicians upon receiving positive reports.

The early prevention of untreated congenital hypothyroidism is the chief aim of our program. In order to achieve this aim most effectively it is our recommendation that endocrinology consultation be sought for those infants identified by screening as being at high risk for hypothyroidism (Figure). This is because the complete, accurate diagnosis and initiation of treatment of this condition are not always straightforward and are best performed under the direction of a qualified pediatric endocrinologist.

The cost of hypothyroidism screening in Minnesota is estimated\* to be \$1.15 per infant, including serum testing and administrative overhead. This cost compares favorably with other large programs<sup>1,10</sup>. The cost of detection of hypothyroid infants is thus only a small fraction of that of caring for mentally retarded individuals.

It should be made clear that the procedures presented here are not regarded as immutable principles and are subject to change and improvement at any time. For instance, the problem of false positive results, of particular relevance to any screening program because of the adverse effect on predictive value, is under close scrutiny. Our initial approach has focused on serum testing of low  $T_4$ -normal TSH babies in order to make sure that any cases of hypothyroidism not grossly observed in the screen would be ascertained without delay or ambiguity. This protocol is obviously not best for sick or premature infants, and, in fact has been chiefly of value in giving an estimate of the incidence of TBG abnormalities. It may be more efficacious to perform repeat filter paper testing, rather than serum testing, on infants with low screening  $T_4$  and normal TSH. We welcome suggestions from concerned individuals regarding the Minnesota newborn screening program.

\*Estimated by the Cost Accounting System of the Association of State and Territorial Public Health Laboratory Directors and the Center for Disease Control.



### Addendum

Since submission of this manuscript a missed case of primary hypothyroidism has been reported to the MDH. The female infant was born in September of 1978, about three months after generalized screening

began in the pilot program. The 2 SD cutoff corresponded to a  $T_4$  of  $3.7 \mu\text{g/dl}$  and the patient's screening value was  $5.3 \mu\text{g/dl}$ . At that time  $7.0 \mu\text{g/dl}$  cutoff was not used.

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### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
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4. Has had a relatively long experience in the field of medical science or a related field.

Nominations for the March, 1981 awards should be sent immediately to:

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Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.

### Cover Photograph

“Minnesota Sunflower”

Mark D. Lindquist, a third-year student at the University of Minnesota School of Medicine, took the photograph of the sunflower featured on the cover in a field near Thief River Falls. His hobby is photography and working with stain glass.

Born in Colorado, he went to Concordia College in Moorhead. His interest lies in emergency or orthopedic medicine, and he expects to practice medicine in Park Rapids, Minnesota. Mark is married and has a small baby daughter.



# Chemical Dependency

## An Evaluation of the Alcoholism Treatment Program at St. Joseph's Hospital

SISTER MARY LEO KAMMEIER, PH.D.\*

**A 12-month follow-up and evaluation study of chemically dependent patients treated in 1975 at St. Joseph's Hospital reports very good maintenance of sequential abstinence, consistent participation in the AA program, and significant improvement in quality of life indicators.**

IN 1975 ST. JOSEPH'S HOSPITAL in St. Paul concluded its first full year of operation of a residential, multidisciplinary treatment program for alcoholism. To determine the effectiveness of this treatment, the hospital contracted with the research department of Hazelden Foundation, a nonprofit treatment center for chemical dependency located at Center City, Minnesota, to evaluate the program.

Hazelden's research team tabulated and analyzed the returns on questionnaires sent to patients at four, eight, and 12 month intervals following treatment. The results of the evaluation are summarized in this article.

### The Patients

During 1975, 386 patients entered St. Joseph's Chemical Dependency Unit. The majority, 287 or 74%, were males; 99 or 26% were females. In general, these people can be characterized as married, predominantly Catholic, skilled, technical or clerical workers who were primarily dependent on alcohol and stayed in treatment 26 to 30 days (22% failed to complete treatment). Average age for women was 40 years; for men 44 years. Of those considered employable (housewives, retirees and others not normally part of the work force were omitted), 30% reported they were unemployed.

Of the original 386, 101 were eventually excluded from the follow up because they stayed in treatment less than seven days (60), refused to participate (17), or could not be located (24).

### Evaluation

Researchers evaluated the treatment program by using follow-up questionnaires, reaction sheets, and personal letters sent at one, four, eight, and 12 month intervals to all patients who completed at least seven days of treatment and who agreed to participate in the follow up.

\*Director of Evaluation and Research Hazelden Foundation, Center City, Minnesota. Posthumous.

Duplicate questionnaires went out to nonrespondents, who were, when possible, contacted by telephone. In addition, in order to provide a reliability check and secure some information on patient nonrespondents, researchers sent comparative questionnaires to confirmants of all participants (confirmants were relatives, AA sponsors, clergymen, etc. recommended by each patient) at eight months and to confirmants of nonrespondents at 12 months. The patient return rate on four month questionnaires was 64%, on eight month questionnaires, 57%, and on 12 month questionnaires, 53%. (In checking on why questionnaires were not returned, researchers discovered 35 more people who had refused to participate but whose names had inadvertently been included in the list of participants). The evaluation measured the effectiveness of the rehabilitation program in relation to three main goals:

1. Total abstinence as a major outcome of treatment for all patients
2. Participation in AA or a comparable self-help group
3. A significant improvement in health and quality of life

### Abstinence

The evaluation revealed that a high percentage of patients responding to the 12 month survey (68.7%) had remained totally abstinent since their release from treatment, while 84%, some of whom had experimented with drinking in the interim, were currently abstinent (Tables 1 and 2). Some patients reported drinking immediately after treatment and then remaining abstinent; some remained abstinent for 10 or 11

**TABLE 1**  
**Drinking Frequency at 12 Months**

	<b>N = 131</b>
<b>Did not drink</b>	<b>68.7%</b>
<b>Only once</b>	<b>2.3%</b>
<b>2 or 3 times</b>	<b>4.6%</b>
<b>4 to 6 times</b>	<b>6.1%</b>
<b>More than 6 times</b>	<b>18.3%</b>



months and then began to drink; and others drank regularly but less frequently and usually reported using smaller amounts of alcohol.

Almost all patients, whether they remained abstinent or not, indicated an improvement in their attitudes toward the need for abstinence. The largest percentage of patients in the abstinent and improved categories indicated "much improved," and even 50% of those with a "not improved" drinking status indicated an improvement in their attitudes toward abstinence. Only five people indicated a "worse" attitude (Table 2).

### **Drug Usage**

A dramatic decrease in the use of drugs other than alcohol also became evident at the 12 month survey. Statistics showed that 22% of the patients reported using drugs inappropriately, and 23% reported using drugs for medical reasons before treatment. A year after treatment, 6% of the patients reported using drugs inappropriately only once and no one reported using drugs as often or more often. Very significant changes occurred, too, in reported medical usage. A slight increase in usage between the four and eight month period dropped to a low of 9% at 12 months (Table 3). These changes in usage suggest that one major benefit of treatment might be a better understanding acquired by the patients about the dangers of indiscriminate drug use, whether prescribed or not. The change in usage might also be related to an improvement of health reported by patients.

### **Participation in AA**

The 12 month survey of Alcoholics Anonymous participants showed, quite simply, that a far greater number of people who attended AA meetings remained abstinent than those who did not attend. It also revealed that a larger percentage of women than men attended meetings regularly; that a relatively high percentage of those who continued to drink (60% of the improved and 40% of those not improved) nevertheless did Twelfth Step work, that is, they helped other alcoholics to overcome their drinking problems; and almost all of those who attended meetings found AA to be of help. Table 4 indicates 67% of the abstinent, 51% of the improved, and 14% of the unimproved reported AA was essential or of much help; and an additional 18% of the abstainers, 22% of the improved, and 43% of the unimproved felt AA was of some help. Many of those patients who continued to drink participated minimally or not at all in AA.

## **Health and Quality of Life**

### *Maturation and Growth*

When surveyed, a vast majority of those in the abstinent and improved categories reported positive changes in relations with others, and the ranking of these changes remained the same for both groups. By contrast, fewer patients categorized as not improved reported positive changes, and their changes ranked in different order (Table 5).

### *Feelings and Attitudes*

Most participants reported improvements in their attitudes and feeling since treatment. An overwhelming 93% of the abstinent, 83% of the improved, and 50% of the not improved reported positive changes in their self image; 92% of the abstinent, 75% of the improved, and 50% of the not improved reported an increase in their general enjoyment of life; and 85% of the abstinent, 60% of the improved, and 38% of the not improved reported improvement in their general physical health. Even at four and eight months after treatment, a sizable majority of patients indicated they had learned new ways to cope with anxiety and depression.

### *Functioning in Skilled Area*

When asked to evaluate themselves in terms of functioning in skilled areas, the majority of those abstinent or improved reported improvement in job performance, ability to handle problems, ability to manage financial affairs, ability to accept help, and ability to give help. Even among those whose drinking habits had not improved, the majority reported improvement in the area of job performance and ability to manage financial affairs, while one third or more reported improvement in other categories. The 12 month survey revealed the unemployment rate had dropped from 30% to 11%. In addition, a high percentage (88% of those abstinent and 79% of the improved) reported positive changes in their spiritual growth.

## **Summary**

Returns of the questionnaires, while considered a good response for this type of survey, remained less than desirable. Nevertheless, out of the information obtained from people who did respond, the following conclusions appear to be valid:

1. The goal of abstinence was achieved by the majority of patients who participated in the follow up.
2. Abstinence is regarded as a valid goal by most of the respondents.
3. Those who reported abstinence were generally



**TABLE 2**  
**Acceptance of Need for Abstinence by Drinking Status**  
**N = 121**

	<u>Abstinent</u>		<u>Improved</u>		<u>Not Improved</u>	
Much improved	67	75.3%	12	50.0%	2	25.0%
Somewhat improved	15	16.9%	8	33.3%	2	25.0%
Same	6	6.7%	3	12.5%	1	12.5%
Somewhat worse	0	0.0%	1	4.2%	2	25.0%
Much worse	1	1.1%	0	0.0%	1	12.5%

**TABLE 3**  
**Frequency of Drug Use at Four, Eight, and 12 Months.**

	<u>4 Month</u> <u>N = 170</u>	<u>8 Month</u> <u>N = 143</u>	<u>12 Month</u> <u>N = 123</u>
Did not use	72.4%	69.2%	84.6%
For medical reasons	21.2%	27.3%	8.9%
Inappropriate use on one occasion	2.4%	.7%	5.7%
Not as often	3.5%	2.8%	.8%
About as often	.6%	0.0%	0.0%
More often	0.0%	0.0%	0.0%

**TABLE 4**  
**Helpfulness of Alcoholics Anonymous by Drinking Status**

	<u>Abstinent</u> <u>N = 89</u>	<u>Improved</u> <u>N = 23</u>	<u>Not Improved</u> <u>N = 7</u>
Essential	51.7%	4.3%	14.3%
Much help	15.7%	47.8%	0.0%
Sometimes helps	18.0%	21.7%	42.9%
Not essential	3.4%	0.0%	0.0%
Do not attend	11.2%	26.1%	42.9%

**TABLE 5**  
**Changes in Relationships with Others by Drinking Status**

<u>Relationship with:</u>		<u>Improved</u>	<u>Same</u>	<u>Worse</u>
<b>Spouse</b>				
Abstinent	N=60	86.7%	6.7%	6.7%
Improved	N=14	85.7%	0.0%	14.3%
Not improved	N= 3	33.3%	33.3%	33.3%
<b>Children</b>				
Abstinent	N=67	92.5%	6.0%	1.5%
Improved	N=17	94.1%	5.9%	0.0%
Not improved	N= 5	40.0%	60.0%	0.0%
<b>Parents</b>				
Abstinent	N=57	75.4%	24.6%	0.0%
Improved	N=14	78.6%	14.3%	7.1%
Not improved	N= 5	40.0%	60.0%	0.0%
<b>Other relatives</b>				
Abstinent	N=80	70.0%	30.0%	0.0%
Improved	N=23	73.9%	21.7%	4.3%
Not improved	N= 6	16.7%	66.7%	16.7%
<b>Friends</b>				
Abstinent	N=87	77.0%	20.7%	2.3%
Improved	N=23	82.6%	13.0%	4.3%
Not improved	N= 7	42.9%	42.9%	14.3%



happier, healthier, and better adjusted than those who continued to drink.

4. Those who had improved their drinking habits were happier, healthier, and better adjusted than those who did not improve.

5. Whatever cause/effect relationship there might be, more persons who attended AA regularly remained abstinent, and almost everyone who participated in AA activities in anyway reported this program as helpful.

In summation, the information obtained from patients who entered the alcohol treatment unit at St.

Joseph's Hospital in 1975 indicates that the established goals of the program were met.

This short report provides information only about the relative effectiveness of the chemical dependency treatment program at St. Joseph's Hospital during its first year of operation. Other information relating to cost/benefits, bed utilization, continuum of care programs, and staff relationships may be secured from the director of the treatment unit.

#### *Minoxidil — A Potent New Antihypertensive Agent — Sweet and Davidman (page 636).*

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### **The Butcher, the Baker, the Candlestick Maker**

The MMA Aux. has recently purchased . . . The Butcher, the Baker, the Candlestick Maker, a 27-minute, 16 mm sound/color motion picture that presents alcoholism as a treatable disease. Its target is educating the public and physicians about the nature of the problem and the urgency of early detection and treatment.

The film includes a cine-play called "I'll Drink to That!" which dramatically illustrates the effect of alcoholism on a couple and the child born to them. The play's dual ending demonstrates the importance of early diagnosis by a physician. It was created by Dr. Joe Norquist, John Goodell and Tom Kohout, produced by Pro-7 Productions, Inc. and sponsored by St. John's Hospital, St. Paul, Minnesota.

The film is available on a loan basis by contacting: Karen Tourdot, Minn. Med. Assn. Aux., 101 E. 5th St., Suite 900, St. Paul 55101. (612) 222-6366

### **Continuing Medical Education**

#### **University of Minnesota**

"Obstetrics and Gynecology: Annual Autumn Seminar" October 15-17

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"Principles of Colon and Rectal Surgery" October 29-November 1

The Division of Colon and Rectal Surgery of the Department of Surgery of the University of Minnesota Medical School presents its annual continuation course at the University of Minnesota.

Contact: Office of Continuing Medical Education, University of Minnesota, Hosp. Box 293, 420 Delaware Street S.E., Minneapolis, MN 55455, (Telephone: 612/373-8012).



# Rheumatology Corner

## HLA and Rheumatic Disease

HARVINDER S. LUTHRA, M.D.\*

**HLA ANTIGENS** are glycoprotein chains expressed on the surface of nucleated cells. Genes which control the expression of these cell surface protein molecules are found in a small segment, called the major histocompatibility complex (MHC), of the short arm of human chromosome 6. Because these antigenic glycoproteins were first demonstrated on leukocytes in man they have been called human leukocyte antigens (HLA antigens). In the human MHC the genes are present in four loci named A, B, C, and D. These autosomal dominant genes exhibit marked polymorphism and at each locus many antigenically different forms have been demonstrated. Each person however has only two genes at each locus, one on each chromosome. A, B and C locus antigens can be detected by serological techniques. Although D locus antigens have been defined by lymphocyte transformation studies recently another serologically defined polymorphic system of alloantigens expressed on B lymphocytes, has been demonstrated. These B-cell alloantigens demonstrate close relationship with D locus antigens and have been named D related or DR antigens.

Since animal studies have demonstrated clear evidence of the role of MHC genes in immune response and disease susceptibility there has been a great interest

to examine the correlation of HLA antigens with human diseases. This has proven very successful and especially so in the rheumatic diseases (Table). The question which needs to be answered is what does this mean and what significance is it to the practicing physician?

Could this be an artifact due to admixture of different populations? Although possible this is not probable since in some diseases, e.g. ankylosing spondylitis 90% of the patients are HLA-B27 positive compared to 8% of the controls, and among young blood bank donors who were B27 positive, 20% were found to have clinical or radiographic features suggestive of ankylosing spondylitis.

Could the HLA antigen association indicate that it is a receptor for the causative organism? This theoretical explanation lacks proof in humans.

Could this association represent linkage disequilibrium between HLA genes and disease susceptibility or disease resistance genes? Currently this is the most popular theory. Recently we have demonstrated a close association of HLA DRw3 with the ability to produce high titer antibodies to native DNA. Sasasaki et al have reported finding an association between presence of an HLA D (HLA-DHO) antigen and the lack of immune response to tetanus toxoid in the Japanese population

TABLE

Disease	HLA type	Frequency		Relative Risk
		Controls	Patients	
Ankylosing spondylitis	B27	8	89	93
Reiters syndrome	B27	8	78	40
Yersinia arthritis	B27	9.4	79	36
Salmonella arthritis	B27	8.6	67	21.5
Psoriatic arthritis				
Peripheral arthritis	B27	8.7	15.5	1.9
Spinal arthritis	B27	8.7	40.2	7
Juvenile chronic Polyarthritis				
Boys with sacroiliitis or spondylitis	B27	8	84	60.3
Other	B27	8	13	1.7
Rheumatoid arthritis	DRw4	15	56	7.2
SLE	DRw2	26.4	57.1	3.7
	DRw3	22.2	46.4	3.0
Either DRw2 or DRw3 or both		48.6	85.7	6.3

\*Assistant Professor of Medicine, Mayo Medical School, Rochester, Minnesota.



studied. These studies suggest presence of immune response and immune suppression genes but further studies are needed to confirm these observations.

In the present state of confusion what significance is the finding of HLA antigen and disease association to the primary physician? This could best be answered as follows: (a) Realization of genetic susceptibility to develop certain diseases. (b) Realization that HLA antigens are normal gene products and although their presence may predispose the individual to certain diseases, only a minority of those inheriting a given antigen will express the association with disease. (c) Realization that the association of HLA antigens, though very strong for some diseases, is not 100% so that individuals lacking these antigens can still develop the disease.

HLA-B27 antigen testing has now become routinely available. One should realize that this test should be used like other laboratory tests, (e.g. IgM rheumatoid

factor, where 5% of normal people are positive, 80% of adult rheumatoid arthritis patients are positive and it occurs in several diseases other than rheumatoid arthritis). Similarly HLA-B27 is present in 8% of the normal Caucasian population, and is present in 70-90% of patients with seronegative spondyloarthropathies. One more point of importance is that the B27 antigen is a gene product and once its absence or presence has been determined, there is no need to repeat this test.

In summary the HLA system has been found to be very complex and polymorphic. Although close associations have been demonstrated between HLA antigens and disease, the mechanism of this association remains speculative. HLA-B27 has shown the strongest association of any to seronegative spondyloarthropathies. In clinical practice its presence or absence should not be the sole criteria for diagnosis of these diseases.

### Continuing Medical Education

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## An Abortion Perspective: Legal Considerations

FRED A. LYON, M.D., F.A.C.O.G.

WITHIN THE VERY recent past, state legislatures and courts have given pregnant women the right to choose whether to legally terminate a pregnancy. There is certainly no unanimity of opinion by the medical profession or society in general as to the wisdom of our legislatures and courts. There is no question however, that these legislative and legal acts have profoundly affected both society and the practice of medicine. A short history of the legal and legislative acts leading to the United States Supreme Court decision of January 22, 1973 will be presented as well as a summary of the more recent court decisions. The medical aspects of abortion will be summarized in a separate paper gathered from the medical experience by the Meadowbrook Women's Clinic, a free-standing, first trimester abortion facility in St. Louis Park, Minnesota.

In the United States, abortion legislation traditionally was the responsibility of each sovereign state. In the nineteenth century, restrictive abortion laws were enacted which remained in force until the middle of the twentieth century. In most states, the law stipulated that a threat to the life of the pregnant woman was the sole legal ground upon which a licensed physician could perform an abortion. In very few states, a serious threat to the woman's health could be considered an indication to terminate a pregnancy.

In 1955, the American Law Institute, composed of eminent jurists, practicing lawyers and professors of law, proposed in its Model Penal Code that physicians should be given the legal right to terminate a pregnancy, if in their opinion, they believed that "there is a substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother, or that the child would be born with a grave physical or mental defect, or if the pregnancy resulted from rape or incest."

It is important to recall that the restrictive abortion statutes enacted in the nineteenth century were passed in order to prevent maternal death since surgical procedures which were performed to produce abortion usually resulted in the death of the mother. Surgical procedures at that time were crude and primitive, no anesthesia was generally available, no blood transfusions were used and antibiotics were unknown.

Abortion was a formidable procedure reserved for those patients who were undoubtedly going to expire even under the best of circumstances. To have liberalized the abortion laws would probably have produced maternal mortalities in greater numbers than allowing pregnant women to die without medical or surgical intervention.

Colorado, in 1967, enacted the first legislation based upon the recommendations of the American Law Institute. Several other states then followed suit and passed similar laws. In 1970, the legislatures of New York, Alaska and Hawaii enacted statutes which no longer specified any indications for the performance of abortion thereby in effect allowing the abortion on demand or request of the pregnant patient. The state of Washington passed similar legislation after a popular referendum of the voters gave approval for such a statute. All of these state legislatures wrote into law that only licensed physicians could perform abortions. It was still a criminal offense for anyone not licensed to practice medicine to terminate a pregnancy. The intent of all of these legislative acts was to deter the practice of performing criminal abortions which resulted in many tragedies to pregnant women including sepsis, trauma and occasional deaths.

On January 22, 1973, the Supreme Court of the United States handed down its monumental decision which in effect held unconstitutional all of the abortion laws of most states. The Court stated that during the first trimester of pregnancy the abortion decision and its effectuation must be left to the medical judgment of the pregnant woman's attending physician. The state could no longer interfere in the decision of the pregnant woman to terminate her pregnancy. Any legal restrictions or obstacles preventing the abortion from taking place were ruled unconstitutional.

In the second trimester, the court ruled, the state may, if it chooses, regulate the abortion procedure but only in ways that are reasonably related to maternal health. The state could however, not interfere with the decision to terminate a pregnancy in the second trimester since it was the right of the pregnant woman to make such a decision.

In the third trimester of pregnancy or after the point of fetal viability was reached, the state was given the

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option of proscribing abortion except where necessary for the preservation of the life or health of the mother.

The Supreme Court, in that same 1973 decision, struck down as unconstitutional many of the procedural provisions which states and hospitals had enacted which had the effect of preventing abortions from being performed. The Court ruled that authorization by hospital abortion committees was unconstitutional. The requirement, as in New York, that a woman must be a resident of the state where the abortion was to be performed was also ruled unconstitutional since no other medical procedure required such a residence requirement and that the only reason for such a requirement was to prevent a woman from having her pregnancy terminated. In effect, all legal and procedural barriers to abortion were now removed. The decision to have a pregnancy legally terminated was left entirely to the pregnant woman and her physician.

By 1980, the decision of the United States Supreme Court has not yet been fully implemented throughout this country. It has been estimated that a large segment of women desiring pregnancy terminations do not have access to such medical services. Legislatures, law enforcement agencies, hospitals, hospital boards and local county welfare boards have deliberately prevented and delayed implementing the law of the land. Legal challenges to such tactics have been almost universally successful but at a tremendous financial cost to the challengers. Laws enacted by state legislatures such as in Minnesota and elsewhere which were intended to restrict the Supreme Court decision of 1973 have been declared unconstitutional. Failure of county welfare boards to remunerate physicians for the cost of such legal medical services to welfare recipients have been challenged successfully.

In June of 1976, the United States Supreme Court affirmed its previous decision on abortion and further clarified the right of a pregnant woman to terminate a pregnancy without interference by the state, her husband or the pregnant minor's parents.

The Court struck down laws that required a husband's consent for an abortion and also parental consent for unmarried women under the age of 18. The Court said that "it cannot hold that a state has the constitutional authority to give the spouse unilaterally the ability to prohibit the wife from terminating her pregnancy when the state itself lacks that right". The Court further explained "that the obvious fact is that when the wife and husband disagree on this decision the view of only one of the marriage partners can prevail. Since it is the woman who physically bears the child and who is more directly and immediately affected by the pregnancy, as between the two, the

balance weighs in her favor".

On the issue of parental consent, the Court ruled that "the state does not have the constitutional authority to give a third party an absolute, and possibly arbitrary, veto over the decision of the physician and his patient. Any independent interest the parent may have in the termination of the minor daughter's pregnancy is no more weighty than the right of the competent minor mature enough to have become pregnant".

The Court also struck down a ban on the use of intra-amniotically infused hypertonic saline as a method of terminating second trimester pregnancies. The majority of the Supreme Court stated that the technique of terminating a second trimester pregnancy by hypertonic saline amnio-centesis is safer in terms of maternal mortality than allowing the pregnancy to continue to term. Data collected by the Center for Disease Control of the Federal Department of Health and Human Services (formerly H.E.W.) for the year 1977 show that 43% of all second trimester pregnancies terminated during that year in this country were done by hypertonic saline infusion. These were for the most part pregnancies of greater than 15 weeks gestation.

Only very recently has data been made available which shows that the newer technique of dilatation and evacuation is the safest method of terminating pregnancies up to 20 weeks gestation. At the time the Supreme Court ruled on the legality of prohibiting hypertonic saline amniocentesis, the justices stated that a prohibition on this method of terminating second trimester pregnancies would be unconstitutional since it could not be considered the sort of reasonable regulation which a state could impose in order to protect maternal health.

The Supreme Court also rejected a provision of the Missouri law requiring physicians to take as much care to preserve the life of the fetus in an abortion as they would in preserving that of a fetus intended to be born or face manslaughter charges. The Court ruled that such requirements would be constitutional only if applied to fetuses beyond the period of viability.

The Court emphatically stated that "whether a fetus is capable of meaningful life outside the womb is a matter of medical judgment, skill and technical ability that cannot be set inflexibly by either courts or legislatures". In view of this most recent ruling, the Minnesota statute passed by the 1976 legislature requiring the presence of two physicians in attendance at the time of a second trimester abortion, has once again been successfully challenged.

In recent years various municipal and state statutes



regulating the practice of abortion have similarly been declared unconstitutional. A Louisiana statute and an Akron, Ohio law have been struck down. Both sought to impose restrictions on abortion practice. Both were declared to be flagrant violations of the rights of patients. Courts have repeatedly stated that legal restrictions cannot be placed on the practice of abortion which single out abortion as a surgical procedure and are not likewise imposed on other minor operations. Higher standards cannot be set for the performance of abortion when compared to other minor surgical procedures.

The Court for example declared as unconstitutional the requirement that a woman having an abortion be forced to sign an informed consent detailing pictorially what a fetus looks like at various stages of embryonic development, be told of serious risks to her health and life, be furnished with statistics as to the risk of infection, hemorrhage and injury. The Court stated that such informed consents are not a requirement for a woman receiving prenatal care and at the time of labor and delivery. To set such requirements for abortion but not for childbirth was an unreasonable demand according to the judges hearing the case. The Court reasoned that such requirements were a form of harassment and were intended to place obstacles in the path of women choosing to terminate a pregnancy.

In March of 1980, U.S. District Judge Alsop ruled that the Minnesota Statute prohibiting payment for abortion services for Medicaid patients was unconstitutional. He ordered the Department of Welfare to honor requests for payment for abortions performed on women receiving State Aid. In July of 1980, the U.S. Supreme Court ruled on the constitutionality of the Hyde Amendment which prohibited the use of Federal monies for abortions except when performed to save the life of the pregnant woman.

By a 5 to 4 decision, the Court declared that federal funding of abortion is not a legal requirement of the constitution. The Court ruled that states may not be required to fund such a legal medical service.

It appears therefore that the Court upholds the principle of a woman's right to choose an abortion but the Justices do not believe that the Federal Government is required to pay for such a medical procedure. Many people are in agreement. They feel that abortion should be available to all who request it. They also feel that public money should not be made available to subsidize such a choice.

There are many others who feel equally strongly that refusal to fund such a legal medical service discrimi-

nates against poor women. They feel that the Court has declared that "all women are equal but some are more equal than others". Those who can pay for such medical care. The Medicaid program certainly pays for other medical services which are not a matter of life and death. Abortion has been singled out. A double standard of medical care has been developed, one for those who can afford to pay and one for those on welfare. Is this discrimination?

It seems clear then that the decision to terminate a pregnancy is now the sole prerogative of the pregnant patient and her physician. The state, at least in the first trimester of pregnancy, cannot interfere with that decision. In the second trimester, the state may only legislate safeguards that are reasonably related to maternal health. The basic decision to terminate a second trimester pregnancy may not be interfered with. It is only in the third trimester that a state may prohibit an abortion but not if it involves the maternal life or health as determined by the physician.

The only consent required to perform an abortion is that of the pregnant woman regardless of her age. The consent of the man involved in the pregnancy is not necessary. The state may not regulate how, where or why an abortion is to be performed unless it is reasonably related to protecting the health of the pregnant woman. All women have the constitutional right to terminate a particular pregnancy for whatever reason; no woman need have an abortion unless she requests it. She cannot be coerced into terminating a pregnancy. No physician is required to perform an abortion if he or she has moral or religious objections to such a legal medical procedure. However, all physicians are given the legal right to terminate a pregnancy upon request by the patient.

Legislative and legal actions thus have basically altered the practice of medicine in the area of reproduction. No longer are physicians forced to refuse to perform an abortion when requested because of the fear of criminal indictment. No longer do physicians have to worry that refusal to perform an abortion will mean that the desperate pregnant woman will attempt a self-abortion or turn her medical care over to a criminal abortionist. No longer will these women be forced by society to continue an unwanted pregnancy or risk criminal prosecution by seeking an illegal abortion. The United States Supreme Court gave women a choice; a choice to continue a desired pregnancy or to terminate it if it is unwanted. Neither patient nor physician is coerced in any way. The Court gave both the freedom of choice.



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*The Minnesota Medical Association,  
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Minnesota Medicine*



## Outpatient Pain Clinic A Long-Term Follow-Up Study

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**A one-to three-year follow-up study of patients with chronic intractable pain who were managed at an outpatient Pain Clinic revealed that such a program can provide many nonsurgical treatment modalities for the control of pain in a cost-effective manner. Both the well-being of the patients and the satisfaction of the participating clinicians were noted. Of patients who responded to the follow-up questionnaire, approximately 40% showed signs of long-term improvement.**

**D**ESPITE CURRENT progress in managing patients with chronic pain syndromes, diagnostic procedures and therapeutic modalities that yield predictable results have not been developed. When the cause of intractable pain is unknown, symptomatic relief of pain and patient comfort become the clinical objectives. Regrettably, even these objectives are not always attainable.<sup>1-3</sup>

Bonica<sup>4</sup> recommended a multidisciplinary approach to chronic pain problems. He proposed that the management of patients with complex pain problems is best achieved through the concerted efforts of a group of specialists who contribute their knowledge and skills for the common goal of making a correct diagnosis and planning the most effective therapeutic strategy.

When we initiated a comprehensive service for the care of patients with intractable pain in 1974, while agreeing with Bonica's concept, we were confronted with the following three problems: (1) how to manage a large number of patients with intractable pain in a cost-effective manner; (2) how to maintain the satisfaction of the participating clinicians; and (3) how to assess the effectiveness of our practice.

At about the same time, an inpatient program to provide the psychologic modalities of intensive psychotherapy and behavior modification was organized in the institution to manage the patients with chronic pain behavior as their predominant problem. A description of that program and its results have been

reported previously.<sup>5,6</sup>

An outpatient program that offers mainly nonsurgical (sensory) modalities, for example, nerve blocks and nerve-stimulating techniques, was established to treat patients with a potential sensory origin of pain. We wish to describe the methods of our outpatient program and to report on the follow-up study of the long-term results of these treatment strategies.

### Method and Materials

All patients were evaluated by a physician in internal medicine, and most were examined by a neurologist. Depending on the nature of the problem, the patients were seen by a psychiatrist, orthopedist, neurosurgeon, or other surgical specialist. Before the visit to the Pain Clinic, the patients had exhausted essentially all available medical and surgical treatment modalities. For the patients with histories of drug abuse, attempts were made to reduce the medications to the minimal requirement. Patients with an abnormal psychologic profile were not excluded from the program.

During the initial visit at the Pain Clinic, the patient was told that the objective of the treatments was to provide symptomatic relief of pain. The absence of a demonstrable pathologic lesion or neurologic deficit explaining the origin of pain did not imply that the pain syndrome was "functional" or "unreal." Where litigation was involved, the patient was informed that failure of the treatments to relieve pain would not mean an entitlement to compensation.

If the patient agreed to proceed, the nature of the treatments and the potential risks were explained. The type of treatment selected was based on the judgment of the attending physician, and some treatment modalities were carried out on a trial-and-error basis. Treatment modalities included assurances and relaxa-

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tion exercises, reduction of analgesic medications, trigger point injections, regional nerve blocks, percutaneous electric stimulation, and acupuncture treatments. The degree of pain was evaluated by the use of a visual pain scale, a listing of the medications used, and the degree of patient physical activity. These data were recorded at the initial visit, six weeks after treatments, and at the follow-up studies.

At the conclusion of treatments, patients were encouraged to reduce the use of medications and to resume their usual activities. If satisfactory pain relief was obtained from the initial treatments but "recurrent" pain developed later, we recommended the initially effective treatment modalities to the referring clinicians in the patient's home community<sup>3</sup> or asked the patient to return to the Pain Clinic for additional treatments. However, every effort was made to avoid reinforcing the pattern of behavior previously associated with the pain. Some patients were referred to physiatrists for physical therapy or exercise programs (or both), which were to be continued after dismissal. After all reasonable physical causes were considered and pursued without undue trauma or harm to the patient, and the pain persisted, the patient was willing to accept a psychologic interpretation of the pain and was referred for psychiatric treatments.

To assess the long-term results of our practice, we conducted a one to three-year follow-up study. A questionnaire was sent to all patients, and the data were compiled by an independent observer.

### Results

During the two years from 1974 through 1976, 725 patients were treated at the outpatient Pain Clinic. Because of death, relocation, or refusal to reply, only 407 patients answered the questionnaire. Data on some of the questionnaires were incomplete, and such data were considered as "not recorded."

When the response and nonresponse groups to the follow-up questionnaire were compared, there were no

specific patterns as to the nature of pain syndromes, therapeutic modalities used, or the psychologic profiles of the patients. However, the nonresponse group had a higher ( $P < 0.01$ ) percentage of patients involved in litigation than the response group (9.9 versus 4.4%). A higher ( $P < 0.0001$ ) percentage of patients in the response group than the nonresponse group had returned for additional treatments (46.7 versus 30.8%).

**TABLE 1**  
Classification of Pain Syndromes of  
Patients Seen at Pain Clinic

Type	Patients	
	No.	%
Headaches	34	8.4
Facial pain	6	1.5
Neuralgia	26	6.4
Myofascial pain	9	2.2
Posttraumatic pain	45	11.0
Postoperative scar pain	58	14.3
Visceral pain (thoracic)	4	1.0
Visceral pain (abdominal)	9	2.2
Postamputation pain	7	1.7
Causalgia	4	1.0
Cancer pain	2	0.5
Low-back pain (sciatica)	110	27.1
Ischemic pain	1	0.3
Spasticity	27	6.6
Unknown origin	64	15.8
Not recorded	(1)	
Total	406	100.0

**TABLE 2**  
Patients' Responses Concerning Duration  
of Pain Relief After Treatments

Duration	Patients	
	No.	%
No relief	125	33.3
Less than 1 wk	40	10.7
1 to 4 wk	54	14.4
1 to 3 mo	54	14.4
4 to 6 mo	35	9.3
7 to 12 mo	31	8.3
No recurrence	36	9.6
Not recorded	(32)	
Total	375	100.0

**TABLE 3**  
Patients' Assessment of Pain Intensity at Initial Visit and Follow-up

Recall of initial pain	Evaluation of pain at follow-up						Total	
	No pain	Mild	Uncom- fortable	Fairly severe	Very severe	Unbear- able	No.	%
No pain	0	0	0	0	1	0	1	0.3
Mild	0	4	0	1	2	0	7	1.8
Uncomfortable	4	5	21	3	0	0	33	8.5
Fairly severe	16	13	18	36	10	2	95	24.5
Very severe	16	23	29	32	75	4	179	46.3
Unbearable	5	14	18	10	9	16	72	18.6
Total	41	59	86	82	97	22	387*	100.0
	(10.6%)	(15.3%)	(22.2%)	(21.2%)	(25.0%)	(5.7%)		

\*Twenty patients had incomplete data.



Only two of 46 patients with intractable pain of terminal cancer survived until the follow-up study was carried out. In the entire response group, 27.1% of the patients had low-back pain (Table 1). While 36 patients (9.6%) experienced no recurrence of pain after treatments, 156 patients (41.6%) obtained relief for one month or longer (Table 2).

Patients were asked to compare the intensity of pain between the times of initial visit and follow-up. Their evaluation revealed that 89.4% had had fairly severe or worse pain at the time of the initial visit. At follow-up, however, the percentage was reduced to 51.9% (Table 3).

Eighty (22.2%) patients started to use new analgesics; but at follow-up, 195 (50.3%) patients used no analgesics or used less than they had before the treatments (Table 4).

The percentage of patients who could perform complete daily activities was higher after the treatments than at the first visit (Table 5). Furthermore, 132 patients (33.6%) were working regularly at follow-up, compared with 70 patients (17.9%) initially (Table 6). There was significant improvement in daily activity (40.1% more active versus 9.8% less active,  $P < 0.0001$ ) and in change in the ability to work (26.2% better versus 8.3% worse,  $P < 0.001$ ).

When they were asked to decide if the treatments at the Pain Clinic were beneficial to them, 174 patients (45.3%) agreed or totally agreed (Table 7).

There was no conclusive pattern in the success rate in relation to the various pain syndromes, treatment modalities used, psychologic profiles, or involvement in legal litigation.

## Discussion

Clinical investigation on complex pain problems has been inconclusive because evaluation of methods for pain control lacks a standardized means for measuring pain. Furthermore, one can never be certain whether the pain is psychologic or physiologic or has a socioeconomic basis.

In this study, success was measured indirectly by estimates of the reduction of pain, the ability to perform daily activities, to retain employment, and a reduction in the use of analgesics.

Moreover, the low rate of response to the questionnaire might not be representative of the entire patient population. Notwithstanding the limitations of this study, the data may be used to assess the effectiveness of our practice.

At follow-up, approximately 40% of the patients had reduced pain intensity and obtained pain relief for

**TABLE 4**  
Medications Used at Follow-Up of  
Patients With Pain Treated in  
Outpatient Pain Clinic

Status at follow-up	Patients	
	No.	%
Medication used initially	387	
Use stopped	102	26.3
Use decreased	93	24.0
Use unchanged	116	30.0
Use increased	63	16.3
None used	13	3.4
Not recorded	(20)	—
New medication	361	
No	281	77.8
Yes	80	22.2
Not recorded	(46)	—

**TABLE 5**  
Patients' Evaluation of Daily Activity

Activity	Initial visit		Follow-up	
	No.	%	No.	%
Normal	32	8.1	83	21.0
Complete, but need more rest	19	4.8	27	6.8
Complete, with some difficulty	97	24.6	118	29.9
Activity very limited	198	50.3	148	37.5
Mostly confined to bed	33	8.4	15	3.8
Totally incapacitated	15	3.8	4	1.0
Not recorded	(13)		(12)	
Total	394	100.0	395	100.0

**TABLE 6**  
Patients' Ability to Work (Job or Household)

Ability	Initial visit		Follow-up	
	No.	%	No.	%
No	122	31.2	103	26.2
Able, but did or do not work	10	2.6	10	2.5
Yes, limited or irregular work	189	48.3	148	37.7
Yes, worked or work regularly	70	17.9	132	33.6
Not recorded	(16)		(14)	
Total	391	100.0	393	100.0

**TABLE 7**  
Patients' Responses Regarding Benefit of  
Treatments at the Pain Clinic

Beneficial	Follow-up	
	No.	%
Totally disagree	78	20.3
Disagree	66	17.2
Cannot decide	66	17.2
Agree	91	23.7
Totally agree	83	21.6
Not recorded	(23)	
Total	384	100.0



one month or longer. The same percentage of patients were more active than at the initial visits and considered the treatments at the Pain Clinic beneficial to them.

The observation that 9.6% of the patients obtained pain relief for as long as three years without recurrence raised the question of whether it was a natural recovery of self-limited problems. This was unlikely because most patients had suffered from pain for an extended period before the treatments.

The temporary relief of pain experienced by some patients might have resulted mainly from placebo effects. Again, it would be difficult to accept this argument, because most patients had been managed without success by many clinicians before their visits to the Pain Clinic. Besides, we tend to agree that if a low-morbidity, low-cost therapy works well enough, it matters little whether it does so by physiologic or emotional mechanisms.<sup>7</sup>

We were aware of the potential risk of reinforcing the abnormal behavior of patients who required additional treatments periodically to obtain relief of pain. However, we often regarded this situation as managing the crisis — acute exacerbations of a chronic pain syndrome. We explained the condition to the patient by means of an analogy to another chronic disorder, for example, diabetes or arthritis. The patients were expected to cope with a new adaptive

state. Dubos once said, "To heal does not necessarily imply to cure. It can simply mean helping people to achieve a way of life compatible with their individual aspirations, even in the presence of continuing disease."<sup>8</sup> Both the patients and the clinicians accepted the reality better that way.

The most important requirements are sustained interest by the physician, a willingness to continue using whatever reasonable measures are available, a lack of dogmatism, and a readiness to review changes and developments in the symptom should they arise.<sup>9</sup>

The role of the physician to control health care cost has been emphasized.<sup>10</sup> We have been able to manage a large number of patients in a cost-effective manner because our time is efficiently utilized and because multiple consultations are requested only for the patients with the most difficult problems. The clinician with a working knowledge of other specialties experiences a sense of satisfaction and a better physician-patient relationship.

Although we are sufficiently encouraged by these results, we realize the need for further improvement. Whether the program contributes sufficient good to society depends on several factors.<sup>11</sup> We must control cost, yet extend the service. We must search for new therapeutic modalities and develop indices whereby the effectiveness of the program can be measured.

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## Patient Reaction to Psychiatric Hospitalization

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Six hundred and ten patients in a private psychiatric hospital completed an evaluation questionnaire designed to inquire into their perceptions of their improvement and what they saw as being most and least helpful to them. A majority of patients perceived improvement in their psychological conditions, relationships with families, relationships with friends and peers, communication skills, morale and self-image. The components of the program perceived to be most helpful were one-to-one sessions with staff members, sessions with doctors, and group therapy. Subjective comments were generally positive, pointing out helpful elements of the program.

FOR MANY YEARS MENTAL health professionals have supported the view that evaluation of psychiatric hospitalization and out-patient treatment is important. The National Institute of Mental Health has set up guidelines for meeting evaluation requirements for federally funded community mental health centers. The Joint Commission for the Accreditation of Hospitals strongly recommends that evaluation programs be set up in all psychiatric hospitals. Health System Agencies (HSAs) are also requiring evaluation components in psychiatry programs. Over the past several years, there have been some studies evaluating outcome, the extent to which patients reach goals set up by staffs (with and without patient input), patient reaction to the physical facilities and degree of helpfulness on the part of various staff members, and the extent to which patient satisfaction correlates with success. The vast majority of these studies have been conducted in university hospitals, V.A. hospitals, state hospitals and community mental health centers. Very little evaluation research has been done in psychiatric hospitals in the private sector, where a major portion of psychiatric care is delivered.

While there is a good deal of acceptance of out-patient individual, marital and family psychotherapy, there continues to be some stigma attached to entering a psychiatric hospital or psychiatric unit in a general medical hospital. It continues to be difficult for many people and their families to accept treatment in psychiatric hospital facilities, even private facilities. Some of the apprehension stems from beliefs that

people who have psychological problems requiring hospitalization are not going to get better. Some of the fear stems from views about what conditions, treatment and outcomes are like in psychiatric facilities. Over the past decade, there has been a great deal of public attention to and criticism of large psychiatric institutions, especially state hospitals. Many people who had been hospitalized for long periods of time were found to be dull and regressed, uninvolved in life. The institutionalization syndrome was identified and described. Following this, there have been major moves throughout the United States to reduce substantially the numbers of people in long-term care psychiatric facilities and return them to the community. There is no question but what stereotypes about what happens to people in large state hospitals have affected views about psychiatric treatment in private, smaller psychiatric facilities as well and contribute to apprehension about hospitalization.

It is, therefore, time to look at the experience of hospitalization in psychiatric hospitals in the private sector. An obvious first step in the evaluation process is to find out what patients' opinions are about the experience of hospitalization. At the time of discharge do they feel better? Has their morale improved? Are their relationships with others less stressful? What aspects of their experience do they believe to have been especially helpful? What do they identify as being not helpful? Whether patients' perceptions of improvement or failure to improve correlate with other measures of outcome such as job performance or opinions of staff and family members about improvement would constitute another step in the evaluation process.

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With the rise of consumerism, there has been a growing concern with the rights of patients and with the experiences they have in hospitals. Opinions of patient consumers provide one source of information to use when considering possible changes in program, physical facilities, subjects for in-service training, emphasis in treatment, etc.

### Study Methodology

A pilot evaluation study directed toward inquiry into patients' perceptions of their improvement and what they saw as being most and least helpful to them was undertaken in the adult psychiatric in-patient units at Abbott-Northwestern Hospital Mental Health Center (the Abbott Division) located in Minneapolis, Minnesota. The study was begun in March of 1977, and tabulations to date were completed in July 1978. An evaluation form was designed to get feedback from patients about their perceptions of improvement, or lack of it, in a variety of areas as a result of their psychiatric hospitalizations. Areas of inquiry were directed to perception of improvement in general psychological condition, relationships with family members, relationships with friends and peers, communication skills, morale and self-image. The second part of the form was designed to get patients' perceptions of which aspects of the hospitalization experience and treatment program were most helpful, and least helpful. Eighteen components of the hospital experience were listed, and the patient was asked to place the number one by the treatment modality that was most helpful, number two by the modality second most helpful, and number three by the third most helpful. They were also asked to check the component of the program least helpful to them. In addition, they were invited to write comments about their opinions. The introduction printed at the top of each evaluation form is as follows: "We are interested in evaluating the treatment program here at the Mental Health Center and would like to get some feedback from you now that you are being discharged. Do not identify yourself. When you have completed these pages, please place them in the envelope that has been given to you and seal it. It will not be opened for several months, at which time we will tabulate the results." On the envelope places were designated for staff to record diagnosis, medications, and a staff consensus rating of degree of improvement in the patient's psychological condition.

Within the twenty-four hour period prior to discharge from the hospital, a staff member gave the evaluation form to each patient. When the form was completed, the patient placed it in the sealed envelope

and returned it to a staff member. The staff member then took the envelope to report where the staff discussed their perceptions of improvement, or lack of it, in the patient's general psychological condition and came to a consensus opinion, which was recorded on the envelope. The envelope was then taken to a central office where it was kept until the time of tabulation. Envelopes were opened at the times results were tabulated first in July 1977 and again in July 1978.

### Description of Psychiatric Setting

The three adult psychiatric units comprise a total of 44 beds and an additional five beds in the intensive care unit. Each patient is admitted by a psychiatrist in private practice who is on the staff of the hospital. The psychiatrist or a clinical psychologist who works in collaboration with the psychiatrist is the primary therapist for the patient. The psychiatrist (and psychologist in some cases) meets each week in a team meeting with unit staff to develop and implement a treatment plan for the patient. Each patient also has a care plan developed by nursing staff with input from the patient regarding problems and goals. Nursing staff is responsible for bringing pertinent data from the care plan as well as daily observations to the team conference. Adjunctive therapy staff are responsible for bringing information regarding the patient's functioning in group therapy, occupational therapy,

The B-3 unit has 14 beds in an open section and an adjoining locked component with 5 beds making up the intensive care unit. The unit is designed for patients with serious psychological problems. At the time of admission to the B-3 unit, many patients are out of contact with reality, often delusional and hallucinatory and would be described as psychotic. (See Table 1 for a tabulation of diagnosis for patients in the study who were hospitalized on B-3). The unit is staffed with 12.4 nurses, 9.8 psychiatric assistants, one half-time group therapist, 1½ occupational therapists, and two recreational therapists. All staff on this unit are specifically assigned there and do not work with patients on other units. Emphasis is placed on providing a low-stress, supportive environment, daily possibilities for one-to-one sessions with staff members, and a structured program composed of occupational, recreational and group therapy. Therapy is directed toward re-motivation, re-socialization, reality orientation, and the problems of daily living. The average length of stay for patients in this study hospitalized on the B-3 unit was 25.97 days.

The Young Adult Unit (YAU) at the time of this study was composed of 16 beds. The unit is designed for people between the ages of 18 and 25. Problems



and issues centering around emancipation, assumption of responsibility, vocational and educational planning and performance, sexuality and identity are addressed. Patients and staff function as a modified therapeutic community; the community processes passes and care plans and takes a role in program planning. Close to half of the patients admitted to the unit during this period had a diagnosis of depression and slightly less than one-quarter (22%) were described as schizophrenic, (Table 1). The average length of stay for patients in this study was 39.69 days. The unit is staffed with 8.4 nurses and 8.4 psychiatric assistants, one occupational therapist and one occupational therapy assistant, one recreational therapist, one part-time movement therapist, and a half time group therapist.

**TABLE 1**  
**Diagnosis**

	B-1	YAU	B-3	Average Total of All Units
Depression	75%	48%	55%	58%
Manic-Depressive Illness	6%	5%	5%	5%
Schizophrenia	3%	22%	22%	16%
Chemical Dependency	2%	5%	1%	3%
Personality Disorder	1%	7%	1%	3%
Anxiety Neurosis	3%	3%	4%	3%
Adjustment Reaction of Adolescence	—	3%	—	1%
Psychotic Depressive Reaction	—	3%	4%	2%
Paranoia	1%	1%	4%	2%
Hysterical Neurosis	1%	1%	1%	1%
Organic Brain Syndrome	—	1%	1%	1%
Anorexia	—	1%	1%	1%
Overdose	1%	—	—	0%
Acute Psychotic Disorder	2%	—	—	1%
Post-Partum Psychosis	1%	—	—	0%
Phobic Neurosis	1%	—	—	0%
Family Problems	1%	—	—	0%
Situational Stress Reaction	1%	—	—	0%
Chronic Back Syndrome	1%	—	—	0%
Psychiatric Evaluation	—	1%	2%	1%

The B-1 unit has 14 beds. Seventy-five percent of admissions are diagnosed as depressive disorders. Few patients on the unit are overtly psychotic, though a minority may have underlying schizophrenic disorders, or fall into the category of borderline state (Table 1). Many persons on the unit are struggling with the loss of important relationships (divorce, separation, death), vocational changes, marital and/or family conflicts, etc. The average length of stay on the B-1

unit for patients in this study was 27.39 days. Most patients can identify their problems, have input into goal-setting, and are able to talk about their problems and feelings. The B-1 unit is staffed by 8.4 nurses and 7.0 psychiatric assistants, one occupational therapist, one recreational therapist, a part-time movement therapist, and two half-time group therapists. In the daily program emphasis is placed on personal growth, communication skills, assertiveness, responsibility for self, and vocational and leisure-time pursuits.

## Results

A total of 610 patients completed the evaluation form: 285 on the B-1 unit; 144 on the YAU and 181 on the B-3 unit.\* See Table 2 for numbers of men and women hospitalized on each unit. As is true of the census of most psychiatric hospitals, almost three-quarters of the total sample were women.

**TABLE 2**  
**B-1, YAU and B-3**

	B-1	YAU	B-3	Total
Male	63 (25%)	52 (37%)	42 (23%)	157 (27%)
Female	192 (75%)	90 (63%)	137 (77%)	419 (73%)
No Response	30	2	2	34
Total				
Questionnaires	285	144	181	610

## Psychological Condition

The first item on the evaluation form is a general one. It states: As a result of my hospitalization, I feel that my psychological condition is (1) Greatly Improved; (2) Considerably Improved; (3) Improved; (4) No Change; (5) Worse; (6) Much Worse. See Table 3 for tabulation of results and Figure 1 for graphed results.

An overwhelming majority (93%) of the 610 patients in all units perceived their psychological conditions as having improved, and more than

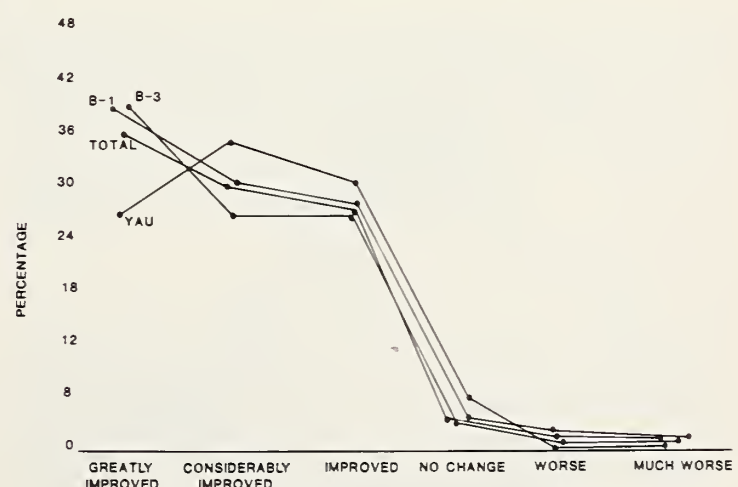


Fig. 1 — Psychological condition.

\*All patients were asked to complete the form prior to discharge. In cases where patients were discharged AMA (against medical advice), the form usually was not completed. An evaluation study designed to inquire into circumstances surrounding AMA discharge is currently being designed.



TABLE 3

A. Psychological Condition	B-1	YAU	B-3	Total
1. Greatly Improved	39%	27%	39%	36%
2. Considerably Improved	30%	35%	27%	30%
3. Improved	26%	31%	26%	27%
4. No Change	5%	6%	5%	5%
5. Worse	0%	0%	2%	1%
6. Much Worse	1%	1%	1%	1%

one-third felt greatly improved. Patients on the B-1 and the B-3 units (39% on each unit) more often considered themselves as being greatly improved than patients on the YAU where 27% saw themselves as being greatly improved. A small minority (8% or less) saw themselves as unchanged or worse.

### Family Relationships

A source of stress for many psychiatric patients lies in relationships with members of their families. Item B is as follows: Relationships with members of my family are (1) Greatly improved; (2) Considerably improved; (3) Improved; (4) No change; (5) Worse; (6) Much worse. See Table 4 for tabulation of results and Figure 2 for graphic results.

TABLE 4

B. Relationships With Family	B-1	YAU	B-3	Total
1. Greatly Improved	18%	11%	24%	18%
2. Considerably Improved	20%	20%	18%	20%
3. Improved	38%	35%	23%	33%
4. No Change	20%	30%	33%	27%
5. Worse	3%	3%	0%	2%
6. Much Worse	0%	1%	1%	1%

Looking at the units combined, slightly more than 70% perceived their relationships with family members as having improved. The improvement, however, was not classified as "greatly" or "considerably" as often was true of general psychological condition.

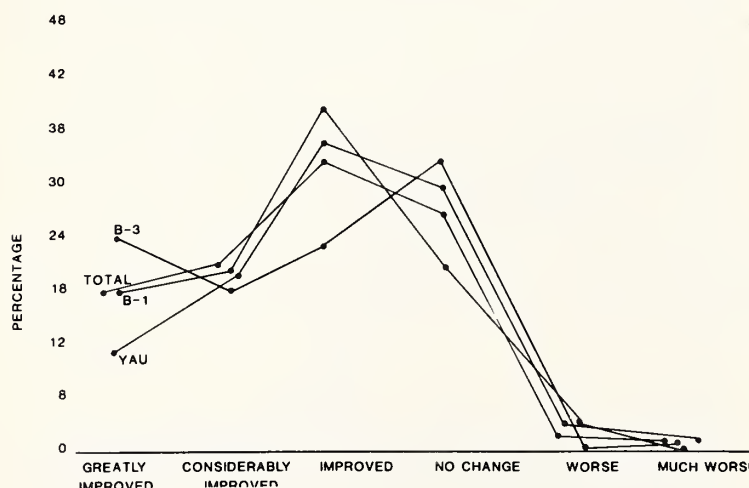


Fig. 2 — Relationship with family.

Twenty-seven percent perceived no change. (It should be noted that not all psychiatric patients have problems in family relationships; therefore a rating "No change" is not necessarily negative.) Patients on B-3 are those with the most serious psychological problems and poorer prognoses. These patients reported improvement in family relationships in two-thirds of the cases. One-third of patients on B-3 perceived no change in family relationships.

While patients in the B-1 unit were most positive of all units in their ratings of improvement in the area of family relationships, only 38% rated the improvement as "great" or "considerable." Twenty-three percent perceived no change or a worsening of relationships. Patients coming to B-1 often have just experienced breakdowns in significant relationships and/or are attempting to cope with divorce, separation, death, family responsibilities, etc. Because these patients are not for the most part psychotic, they are able to talk about their relationships, set up goals for changing them, and work through feelings about past and present relationships. On the B-1 unit relationships with family members are explored and addressed in psychotherapy with the primary therapist, one-to-one sessions with various staff members, and in group therapy. The ratings, while generally positive, suggest the possibility of programmatic changes in the direction of providing family therapy as a part of the treatment program.

On the YAU there was the perception of generally less improvement in family relationships with only 11% seeing great improvement in this area and one-third rating no change or a worsening of these relationships. On this unit the emphasis is often on helping young people to emancipate from parents and to take responsibility for their own lives. For this reason there may be less emphasis on working to improve family relationships. These patient perceptions may quite accurately reflect few marked improvements in family relationships. They may also be associated with distancing from the family during an emancipation process. Whether or not this stems from unit philosophy and program should be further investigated.

### Relationships With Friends and Peers

Item C is as follows: Relationships with friends and peers are (1) Greatly improved; (2) Considerably improved; (3) Improved; (4) No change; (5) Worse. See Table 5 for tabulation of results and Figure 3 for graphed results.



TABLE 5

C. Relationships With Friends	B-1	YAU	B-3	Total
1. Greatly Improved	17%	12%	16%	16%
2. Considerably Improved	24%	24%	22%	23%
3. Improved	35%	34%	31%	34%
4. No Change	21%	25%	30%	25%
5. Worse	2%	3%	1%	2%
6. Much Worse	0%	1%	0%	0%

Relationships with friends, while important, are probably not as significant in most cases as sources of stress as are relationships with family members. Also, these relationships are not as often the subjects of conflicts dealt with in group and in individual therapy. Here, as was true of the YAU unit responses to the family items, the smallest percentage (12) rate their relationships with friends as having greatly improved, though a majority perceive considerable or some improvement. Further investigation of the importance of this category should be conducted.

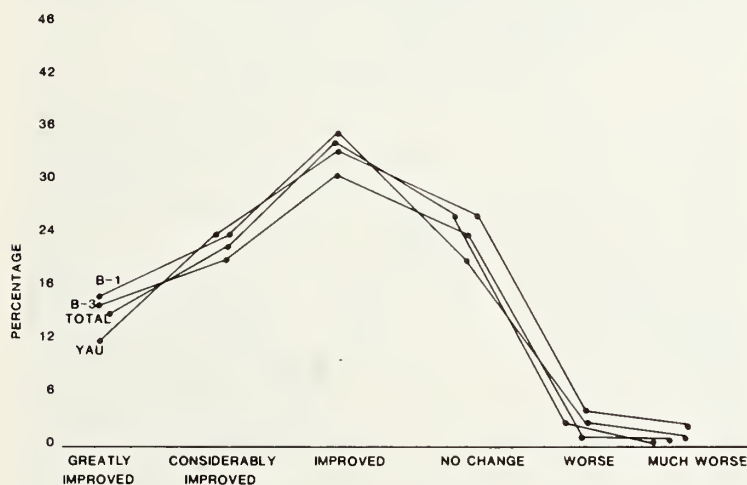


Fig. 3 — Relationship with friends.

### Communication Skills

Item D is as follows: My communication skills are: (1) Greatly Improved; (2) Considerably improved; (3) Improved; (4) No change; (5) Worse; (6) Much worse. See Table 6 and Figure 4 for results.

Many people with psychiatric problems have poor communication skills. Some are so preoccupied with their own discomfort or are so fixed in their patterns of relating that they fail to listen to others. Some are able to acknowledge their feelings, attitudes and opinions, but are too fearful to express them. Still others make erroneous interpretations and cling to them because they do not seek or obtain feed-back from others. On all units the theme of many one-to-one sessions with a variety of therapists and group adjunctive therapy sessions as well is communication. One goal of treatment often is improvement in communication

skills. In this study a vast majority of patients on all units perceived improvement in their communication skills. Patients on the YAU perceived the most improvement. Patients on the B-1 unit perceived the next most improvement, and patients on the B-3 unit the least improvement.

TABLE 6

D. Communication Skills	B-1	YAU	B-3	Combined
1. Greatly Improved	15%	21%	21%	18%
2. Considerably Improved	31%	30%	20%	27%
3. Improved	41%	37%	40%	40%
4. No Change	11%	11%	18%	13%
5. Worse	2%	1%	1%	1%
6. Much Worse	0%	0%	0%	0%

Since patients on the B-3 unit are the most disturbed and have the most difficulty in reality-testing, this perception may be quite accurate. Also, because patients on the B-1 unit and YAU are most intact and more verbally appropriate, they are better able to participate in sessions, programs and projects designed

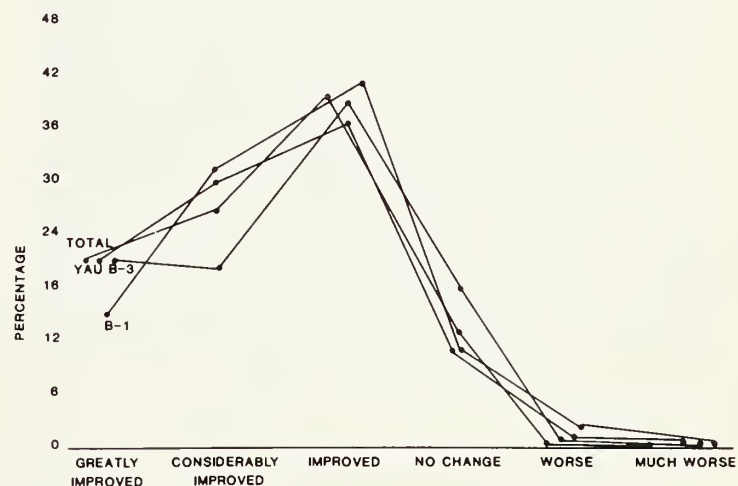


Fig. 4 — Communication skills.

to help them in this area. It is interesting to note that patients on all units perceived more improvement in their communication skills than in their relationships with family and friends. This difference is especially striking on the B-1 unit and YAU.

### Morale

Item E is as follows: My morale is: (1) Higher; (2) Unchanged; (3) Lower. A strong majority of patients on the combined units, 82%, rated their morale as being Higher at the time of discharge. A striking 85% of patients on B-1 rated their morale as higher. See Table 7 and Figure 5 for results.



TABLE 7

E. Morale	B-1	YAU	B-3	Combined
1. Higher	85%	80%	79%	82%
2. Unchanged	11%	17%	18%	14%
3. Lower	4%	3%	3%	3%

It is probably fair to say that most people entering psychiatric hospitals have low morale. Many have been admitted because of major symptoms of depression. In this study, 58% of all patients had a diagnosis of depression. Many of those with other diagnoses also had feelings of depression that were uncomfortable and disturbing. Some were pessimistic because of losses they have experienced. Others were discouraged because the current admission is one of a series, and they despair at the recurrence of their difficulties. Still others had low morale because their problems culminated in admission to a psychiatric hospital. It is perhaps only persons in manic states or those who are disoriented and unaware of the significance of their conditions who do not have low morale at the time of admission. A psychiatric hospital experience that results in no perceived change in morale or a lower morale would certainly not be successful. The successful treatment of depressive disorders must by definition result in improved morale. And successful treatment of all patients who enter with feelings of depression (even though depression does not constitute the primary diagnosis) must lead to improved morale if patients are to be discharged feeling more comfortable and better able to function in families at work, etc. It is thus a sign of success of this experience and program that a large majority of patients experienced improved morale.

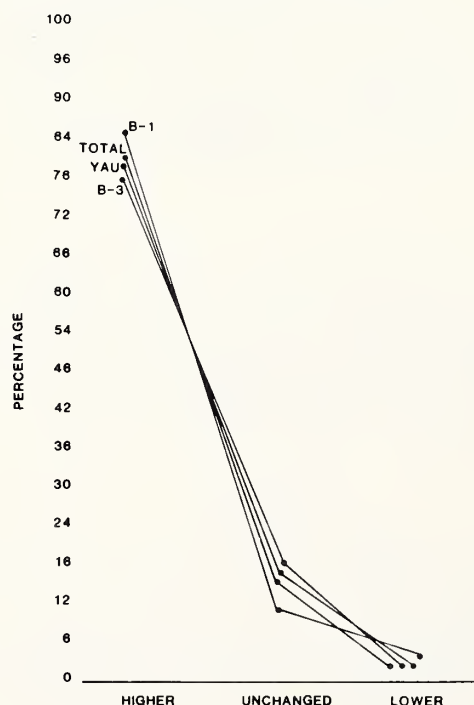


Fig. 5 — Morale.

## Self Image

Item F is as follows: My self image is: (1) Greatly improved; (2) Considerably improved; (3) Improved; (4) No change; (5) Worse; (6) Much worse. Eighty-seven percent of the total number of patients rated themselves improved or better. See Table 8 and Figure 6.

TABLE 8

F. Self-Image	B-1	YAU	B-3	Total
1. Greatly Improved	21%	24%	26%	23%
2. Considerably Improved	32%	30%	27%	30%
3. Improved	35%	32%	33%	34%
4. No Change	8%	9%	12%	10%
5. Worse	3%	4%	2%	3%
6. Much Worse	0%	1%	0%	0%

A slightly larger percentage on the B-3 unit (not statistically significant, however) saw their self-concepts as unchanged. Fewer than one-third of patients on all units perceived their self-images as being Greatly Improved.



Fig. 6 — Self-image.

## Ranking by Judges

As noted above, patients were asked to check on a list of components of the hospital experience, which component was first, second and third most helpful to them (Table 9). Not all of the 610 patients completed this section of the evaluation form. In their subjective comments, a number of patients said that the total program was helpful and that it was difficult to identify what was most helpful. For example, one patient wrote, "Somehow the combination of medication, doctor, the program and time plus my active and enthusiastic participation had remarkable results. What was most important or least important is of little consequence." Another wrote, "To me it seemed like a well-rounded program."



There was a total of 1209 responses, out of a possible 1830, to this part of the evaluation form. It should be noted that no one component of the program received an overwhelming majority of positive responses, again suggesting that it is the total experience and a combination of program elements that is perhaps most highly valued.

The three components of the program perceived to be most helpful were one-to-one sessions with staff (18% of responses), sessions with doctor (17%) and group therapy (17%). It is interesting to note that these three top-rated components all fall into the category of verbal therapies. They all involve a "talking" relationship with a person or persons about the patient's feelings, attitudes, experiences, etc.

The components of the program that are rated next most valuable are medications (9%), interactions with patients (9%) and community support (8%).

**TABLE 9**  
**Most Helpful**  
**B-1, YAU, B-3 Combined**  
**(Total of 1st, 2nd & 3rd Choices**  
**Based on 1209 Responses)**

Group Therapy	206	=	17%
One-to-one Sessions with Staff	215	=	18%
Medications	112	=	9%
Interactions with Patients	107	=	9%
OT	52	=	4%
Personal Growth	30	=	2%
Goal or Task Group	21	=	2%
Sessions with Doctor	206	=	17%
Community Support	101	=	8%
Sexuality Sequence	6	=	0%
RT in Hospital	18	=	1%
RT Outside Hospital	28	=	2%
Special Programs	6	=	0%
Medical Care of Physical Condition	17	=	1%
Vocational Counseling	3	=	0%
Community Meetings	12	=	1%
Movement Therapy	60	=	5%
ECT	11	=	1%

Two of these components have to do with relationships among patients.

Two major components of most psychiatric hospital treatment programs, Occupational Therapy and Recreational Therapy, were not judged by many patients to be among the most helpful parts of the experience.

Patients were also asked to indicate what component was the least helpful (Table 10). Three-hundred and seventy-five of a possible 610 patients completed this part of the evaluation form. A number of people indicated that they perceived the program as a whole to be helpful and could not identify what was "least helpful." Community meetings (18%) and Occupational Therapy (13%) were most frequently identified

**TABLE 10**  
**Least Helpful**  
**B-1, YAU, B-3 Combined**  
**Total Responses = 375**

Group Therapy	26	=	7%
One-to-one Sessions	8	=	2%
Medications	24	=	6%
Interactions with Patients	7	=	2%
OT	48	=	13%
Personal Growth Group	8	=	2%
Goal or Task Group	15	=	4%
Sessions with Doctor	14	=	4%
Community Support	3	=	1%
Sexuality Sequence	32	=	9%
RT in Hospital	17	=	5%
RT Outside Hospital	9	=	2%
Special Programs	3	=	1%
Medical Care of Physical Condition	14	=	4%
Vocational Counseling	21	=	6%
Community Meetings	66	=	18%
Movement Therapy	34	=	9%
ECT	26	=	7%

as "least helpful."

### Staff Evaluation

As noted above, staff members on each unit met at the time of discharge for each patient and reached a consensus opinion regarding the degree of improvement shown. See Table 11 and Figure 7.

While the staffs believed that the vast majority of patients had improved and that none was worse, they were more conservative in their ratings of Greatly Improved and Considerably Improved than were the patients themselves. The staff on B-3, where more severely disturbed patients are hospitalized, saw the most striking improvements. Patients on this unit are often acutely psychotic at the time of admission and as they recover from this state, behavior changes are often dramatic. On B-1 and the YAU units patients on the average show less impairment in their functioning and

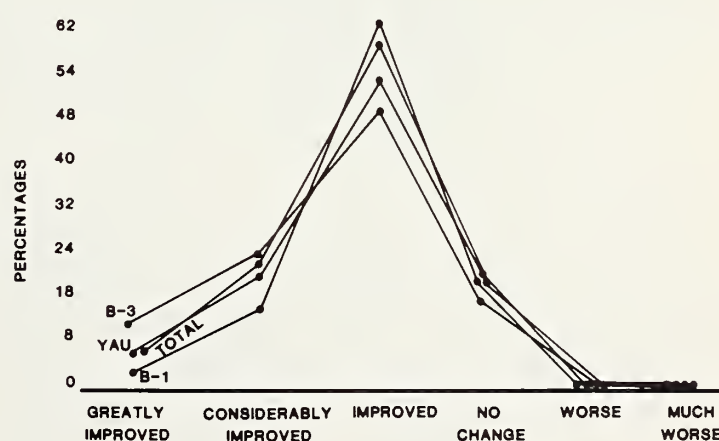


Fig. 7 — Staff evaluation



are perceived by staffs on these units as having improved, but not as strikingly as on B-3. In the future, research should be directed toward those patients who are perceived as not having improved.

### Subjective Responses

Patients were also invited to write comments, and a blank page was provided for this. Two judges read the comments and independently rated them as favorable (+), mixed or neutral (0), or negative (-). See Table 12 for numbers and percentages of patients' responses for which there was agreement between judges. Considering the total number of patients on all units who wrote comments, the two judges reached agreement in 89 percent of their ratings.

On the B-1 unit 146 out of 285 patients wrote comments. The comments were generally highly favorable. Of the 124 comments on which the judges reached agreement, 114 (or 92%) were classified as positive (+), 6 (5%) were classified as negative (-), and 4 (3%) were classified as mixed or neutral (0). Phrases such as "fantastic experience," "an excellent program," "happy that I could participate in such a constructive program," were typical. A characteristic paragraph is as follows: "My stay on B-1 was a unique and extremely positive experience. I've sought help several times without any measurable success. I feel I've changed and grown more at B-1 than at any time in my life. The combination of structured group therapy, movement therapy, and one-to-one sessions with a

psychiatrist with the less structured interactions with staff and other patients provided an effective program for me. I feel for the first time I have begun the process of growth and change which will help me eventually overcome my problem with depression."

An example of comments classified as "mixed" is as follows: "I really feel that all the therapies were helpful — just some more than others. The activities sometimes fell too close together; i.e., R.T. or O.T. after a heavy group session. It was sometimes difficult to try to examine and explore things about myself and others when one activity fell close to another. Sometimes it was even detrimental in that I would forget something I wanted to remember. Also, too, it was difficult for me to go from tears to dancing. For me the pace during the days here was a little fast. However, I invested myself and I feel I received a tremendous amount of insight here. The groups that were hardest for me I liked the most. Praise to the staff — and patients — on B-1."

A characteristic example of the few comments classified as negative is, "Schedule should be more consistent. When something is cancelled, patients should be informed. Lack of organization is very confusing for staff and patients. Staff should give more direct feedback to patients. Staff should read the P.I. (personal inventory) before getting into "helping" discussions with patients. My care nurse was asking the same questions after five days. It was obvious that she had not listened to me and she had not read my P.I."

**TABLE 11**  
**B-1, YAU, and B-3**

	<b>B-1</b>	<b>YAU</b>	<b>B-3</b>	<b>Total Average All Units</b>
<b>Average Length of Hospital Stay</b>	<b>27.39</b>	<b>39.69</b>	<b>25.97</b>	<b>31.02</b>
<b>Staff Evaluation at the Time of Discharge</b>	<b>days</b>	<b>days</b>	<b>days</b>	<b>days</b>
<b>1. Greatly Improved</b>	<b>3%</b>	<b>6%</b>	<b>11%</b>	<b>7%</b>
<b>2. Considerably Improved</b>	<b>18%</b>	<b>18%</b>	<b>23%</b>	<b>20%</b>
<b>3. Improved</b>	<b>61%</b>	<b>55%</b>	<b>51%</b>	<b>56%</b>
<b>4. No Change</b>	<b>18%</b>	<b>20%</b>	<b>16%</b>	<b>18%</b>
<b>5. Worse</b>	<b>—</b>	<b>—</b>	<b>—</b>	<b>—</b>
<b>6. Much Worse</b>	<b>—</b>	<b>—</b>	<b>—</b>	<b>—</b>

**TABLE 12**  
**Ratings of Judges**

	<b>No. of Patients</b>	<b>Rating Agreement</b>		<b>Rating Disagreement</b>	
		<b>No.</b>	<b>Percentage</b>	<b>No.</b>	<b>Percentage</b>
<b>B-1</b>	<b>146</b>	<b>124</b>	<b>85%</b>	<b>22</b>	<b>15%</b>
<b>YAU</b>	<b>54</b>	<b>48</b>	<b>89%</b>	<b>6</b>	<b>11%</b>
<b>B-3</b>	<b>59</b>	<b>56</b>	<b>93%</b>	<b>4</b>	<b>7%</b>
<b>Total</b>	<b>259</b>	<b>228</b>	<b>89%</b>	<b>32</b>	<b>11%</b>



It is obvious that the vast majority of patients on B-1 felt very good about their experiences in the hospital and were very highly complimentary about staff and programs.

On the YAU 54 out of 144 patients wrote comments. Of the 48 comments on which the judges reached agreement, 45 (94%) were classified as positive (+) and 3 (6%) were classified as negative (-). This unit had the largest percentage of favorable comments and the smallest percentage of unfavorable comments. An example of a positive comment is as follows: "The program helped me become aware and look into various approaches and insights to my problems. I rate the program very highly and feel it was extremely beneficial to me. I also made some close friendships and grew to be quite dependent on the hospital, it being such a safe place, a safe environment. I feel like I have a good, strong beginning to approaching my problems in 'the big world,' whereas before I came into the hospital I felt I had nowhere to turn."

An example of a comment written by a patient on the YAU classified as "mixed" follows: "This program has been helpful to me, although I know I am leaving too early. But maybe I am not. I really don't know. I just want to get out and apply the things I have learned. And I know I can make it now if I choose to. And thank you everyone for your help. I am improved. Even if O.T. and R.T. are part of the program, I don't feel patients should have to go if they wish not. They should get out of the program what they want. And I feel one-to-one should be available for these patients who do not wish to go to Movement, R.T. and O.T. People have different problems and should be dealt with differently."

An example of one of the very few negative comments is as follows: "Staff spent too much time in the back room when people were being late. It was frustrating because there wasn't anything really specific to do about it."

On B-3, 93% of the comments were rated as favorable (Table 12). A total of 60 patients out of a possible 181 wrote comments. Of the 56 comments on

which the judges reached agreement 50 (89%) were classified as positive (+), 2 (4%) were classified as negative (-), 4 (7%) were classified as mixed or neutral (0). A characteristic example of a favorable comment written by a B-3 patient is as follows: "Thanks to all those who have helped me and listened to my problems. I feel that just talking to the patients has helped me the most, the feeling that I'm not the only one with this kind of problem. The games I participated in helped me to relax. I took an awful lot of hurt and anger out on that volleyball. Group therapy gave me new ways and ideas of coping with my problems. I have learned to hold my temper and express it constructively."

An example of a comment written by a patient on the B-3 unit classified as "mixed" is as follows: "Needed more therapy with doctor. Incidents that were happening were not gotten to the root of — or explained properly."

A characteristic example of one of the very few negative comments follows: "I am not ready to go home yet."

In summary of the subjective comments made by patients on all these units, it can be said without doubt that the vast majority were highly positive. The few criticisms that were made should be examined and discussed.

## Summary

Six hundred and ten patients in a private psychiatric hospital completed an evaluation questionnaire designed to inquire into their perceptions of their improvement and what they saw as being most and least helpful to them. A majority of patients perceived improvement in their psychological conditions, relationships and families, relationships with friends and peers, communication skills, morale and self-image. The components of the program perceived to be most helpful were one-to-one sessions with staff members, sessions with doctors, and group therapy. Subjective comments were generally positive, pointing out helpful elements of the program.

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# Minnesota Medical Association

from

## *Division of Socio-Economic Affairs*

James H. Sova, Assistant Executive Vice President

Lynn R. Gruber, Director, Department of Medical Services and Research

George C. Lohmer, Jr., Director, Department of Health Planning

Charles W. Wiger, Director, Department of Legislative Affairs

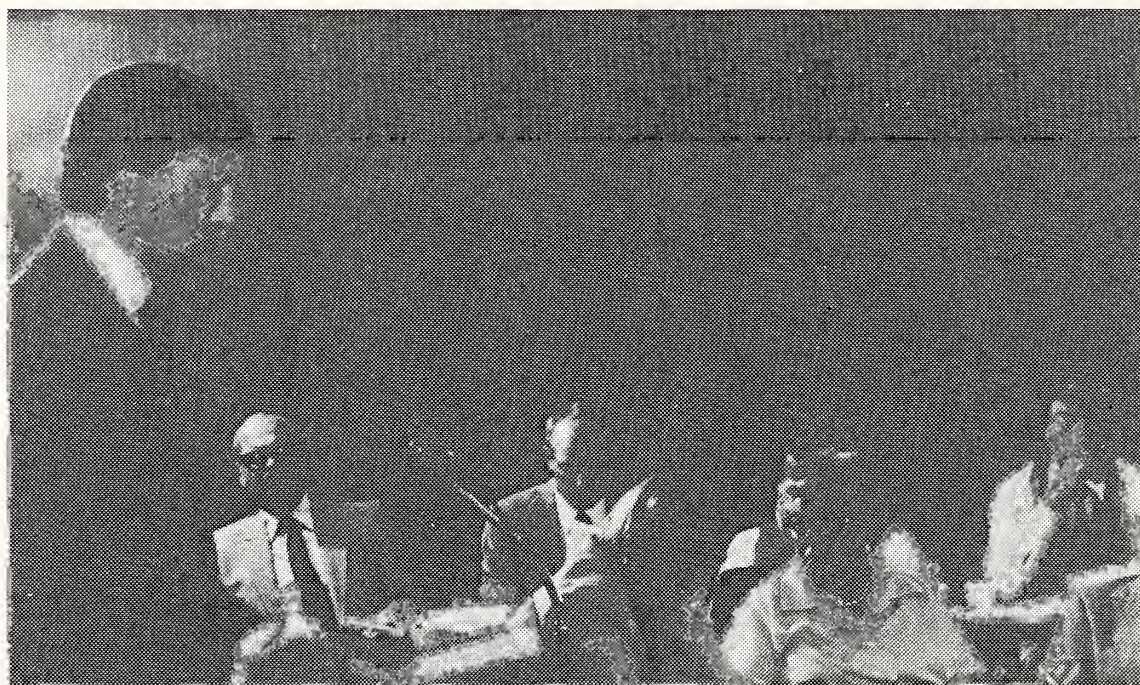
### Health Planning

#### *Physicians Metro Health Force opposes Metro Health Board's Report on the Designation of Hospital Specialty Services*

The Metropolitan Health Board and area hospitals have developed a hospital long range planning process. The objective of this process, based on the assumption that cost-savings would result, was the reduction of some 2,000 excess hospital beds and the consolidation, merger, or closure of hospital specialty services in the areas of pediatrics, perinatal, stratified cardiac care (open heart surgery and cardiac catheterization), megavoltage radiation therapy, and computerized tomography. The Health Board's Report on Phase III of this long range planning process contains recommendations of which hospitals should provide these specialized services. The report is titled: "Phase III Designations: A Report on Specialized Hospital Services for the Twin Cities Metropolitan Area Under the Long-Range Hospital Plan."

On July 31, the Metro Health Board held a public hearing to listen to comments on their "Phase III" report. Over 30 speakers provided their views. The vast majority felt that the designation of specialty services was inappropriate and represented a change from the Health Board's prior philosophy of cooperative planning with the area providers into a regulatory model.

Dr. A. Stuart Hanson, Chairperson of the PMHF, emphasized in his testimony the long cooperative relationship the area's providers, and physicians have had with the Health Board. He stated that their goal of quality, cost-effective care was a high priority of the PMHF. He went on to state that "Previous activities of the Health Board are acting as a



Dr. A. Stuart Hanson, (Chairperson, PMHF) delivers his testimony at the Health Board's public hearing on hospital designation. To Dr. Hanson's left is Charles R. Weaver, (Chairman, Metro Council), seated with other Metro Council and Health Board members.



catalyst to 'nudge' the system in the direction of quality, cost-effective care. However, we draw the line at the designation of specialty services. We feel that the Phase III designations of specialty services are inappropriate, inadvisable, and detrimental to patient care.' Dr. Hanson raised questions about the viability of hospitals without pediatric and obstetric units; why previous community input was not used; and did the Health Board intend to remove flexibility from the hospital system.

Dr. John B. Coleman, former Chairperson of the PMHF, and present Chairperson of the MMA's Committee on Health Planning, presented his own perspectives on the "designation" process. Some other physicians presenting testimony included: William Krivit, M.D., Stuart V. Thorson, M.D., James H. Moller, M.D., James K. Struve, M.D., Neal L. Gault, Jr., M.D., Joseph P. Connolly, M.D., Theresa A. Baker, M.D., John A. Culligan, M.D., and Mary H. Donohue, M.D.

### **Medical Services and Research**

The noticeable increases in the cost of health care during the past few years have recently compelled major corporations and third party payers of health care to scrutinize the specific health care benefits which they currently provide for their employees or subscribers for ways to achieve cost containment in health benefits without risking quality of care.

One institution, Blue Cross/Blue Shield of Minnesota (BCBSM), has received pressure from some of its larger subscriber groups to create new health benefits which address the issue of containing costs and/or decreasing the amount of money which industry now pays out to its employees for health care. Since April, 1980, BCBSM has directed its staff to begin the design of new cost containment programs to combat the high cost of health care. While the Board of Trustees of BCBSM has not yet approved any major changes in benefit packages, BCBSM staff has suggested that an emphasis be placed on: utilization review of a patient's experience in the hospital, more frequent use of outpatient hospital or doctor office facilities for ambulatory surgeries, pre-authorization for inpatient chemical dependency treatment, home health care alternatives, and related health education for subscribers. MMA is supportive of cost containment efforts but has strongly stressed that utilization review and medical necessity determinations be made through physician peer review mechanisms as conducted by the appropriate PSRO. Future developments and discussion of these programs will be shared by BCBSM Staff with the MMA Committee on Medical Service.

Representatives from the Honeywell Corporation recently visited the MMA Staff to explain Honeywell's interest in decreasing or at least containing the rapid rate of corporate expenditures for health benefits, and to ask the medical community for assistance in this effort. Honeywell is now in the planning stage of identifying a utilization review program to help analyze its employees' hospitalization experiences. In addition, it hopes to create incentives for its employees to obtain more health services on an out-patient basis and to receive chemical dependency treatment in non-hospital based facilities. Honeywell is seeking the assistance of the MMA in developing guidelines to individualize the recovery timetable for temporarily disabled employees.

The Minnesota Department of Corrections contacted the MMA to ask its help in designing a four-hour curriculum for jailers on the administration of medication to inmates in county jails. The Committee on Medical Service responded by creating a task force comprised of Robert Derro, M.D., Vince Hunt, M.D., Annette Sova, R.N., and Charlotte Weiss, R.N., to critique the American Medical Association's course material on the administration of medicine as used in its jail health program for possible application to the Minnesota jail system.



### Legislative Affairs

Legislative strategies for the 1981 Session received close scrutiny at the July 28 meeting of the Committee on Legislation. One key issue promises to be amendment of the Preschool Screening Program. The Committee discussed implementation of the Board of Trustees policy adopted on the recommendation of the Subcommittee on Preschool Screening that provisions of the 1977 law relating to Phase II components be deleted. These include laboratory tests and nutritional and physical assessments. Data does not support the benefits to be obtained from expenditures on this program part.

Department attention is focused on interim activity of various legislative committees. Subcommittees of the House Health and Welfare Committee are discussing methods to decrease the incidence and harm resulting from teenage pregnancies as well as considering a revised form of amendments to the Minnesota Hospitalization and Commitment Act. Dr. John Mulvahill, Resource Group on Psychiatry Chairman presented MMA testimony on the MHCA stressing MMA opposition to unlimited access by patients to their medical records. MMA supports most other provisions of the bill which increase the procedural safeguards to the patient, his physician and attorney.

Health Care Subcommittee members received testimony from the Citizens League regarding its study of chemical dependency. The report released prior to the hearing criticizes the treatment of chemical dependency in Minnesota. A key area of concern is the cost of hospital based treatment. One section of the report stated that physicians were not sympathetic to the chemical dependency problems of their patients. MMA study and response to the report will be delivered soon.

Minnesota  
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Minnesota  
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#### \*\*\*ANNOUNCE\*\*\*

#### Safe, Practical Radiology for X-ray Machine Operators

In response to concerns expressed in the Minnesota Legislature and from other sources about radiation safety and x-ray machine operator training, a continuing education program for your x-ray machine operator will be offered.

Important areas to be covered are: radiation safety; exposure; proper positioning; processing; and patient communication. Registration fee is \$30.00.

Minneapolis — October 4  
At St. Louis Park Medical Center  
8:00 A.M. — 4:30 P.M.

Willmar — October 18  
Rice Memorial Hospital  
8:00 A.M. — 4:30 P.M.

Mankato — November 1  
St. Joseph's Hospital  
8:00 A.M. — 4:30 P.M.

Albert Lea — November 15  
Naevie Hospital  
8:00 A.M. — 4:30 P.M.

Watch your mail for complete information and registration materials or contact: Douglas Bruce, Program Coordinator at 612/340-8561, Foundation for Health Care Evaluation, 20 Washington Avenue, S., Minneapolis, MN 55401.



# Minnesota Medical Association

## CME in Minnesota

Beginning with this issue, the Department of CME and Program Services will regularly publish a listing of CME programs to be offered in Minnesota. This effort is under the direction of the MMA Committee on Medical Education. The listing is limited to courses of four hours' duration or more. The calendar does not include regular in-house hospital staff programs or short lectures presented at medical society meetings. Information on accredited hospital medical education programs may be obtained by calling the MMA office.

*An ongoing calendar of scheduled CME programs as well as important holidays, state and national medical meetings and other important dates extending into the future will be maintained in the MMA office. CME planners are encouraged to contact the office when planning future programs so as to avoid scheduling conflicts.*

Information for each entry below is arranged as follows: Name of program; Primary sponsor; Location; Date; Contact person.

Stuart V. Thorson, M.D., Chairman  
Subcommittee on CME Resources

### September, 1980

1980 Meeting; Minn-Dak-Man. **Orthopaedic Society**; Duluth; Sept. 12-13; CONTACT Peter L. Boman, M.D., 400 E. 3rd St., Duluth, MN 55805, 218/722-8364.

**Clinical Microbiology Reviews**; Mayo Foundation; Mayo Clinic, Rochester; Sept. 15-17; CONTACT Postgraduate Courses, Room 720, Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Uroradiology**; U of M Medical School; U of M Mpls.; Sept. 15-19; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Basic Cardiac Life Support**; North Memorial Medical Center; North Mem. Med. Ctr., Mpls.; Sept. 17-18, Oct. 15-16, Nov. 12-13, Dec. 10-11. CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**The Aging Heart**; U of M Medical School; U of M Mpls.; Sept. 17-18; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Cancer Reviews**; Mayo Foundation; Mayo Clinic, Rochester; Sept. 18-19; CONTACT Postgraduate Courses, Room 720, Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Medical Directors Fall Meeting; Monitoring Quality of Care**; U of M Medical School; U of M Mpls.; Sept. 19; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Psychiatric Aspects of Aging**; North Memorial Medical Center; North Mem. Med. Ctr., Mpls.; Sept. 19; CONTACT James Garvey, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

Annual Meeting — **Managing Public Health Services in the 1980's**; Minnesota Public Health Association; Grandview Lodge, Brainerd; Sept. 24-26; CONTACT John Cushing, VP, Corporate Development, Metropolitan Medical Center, 900 S. 8th St., Mpls., MN 55404, 612/347-4414.

**Third Annual Trauma Seminar**; U of M Medical School with Hennepin Co. Med. Ctr.; Hennepin Co. Med. Ctr., Mpls.; Sept. 25-26; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**2nd Annual Adolescent Medicine and Health Care Conference**; U of M Medical School with MN Chapter, Amer. Acad. of Pediatrics; U of M St. Paul; Sept. 25-26; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Central Association of Obstetricians and Gynecologists**; Radisson South, Mpls.; Sept. 25-27; CONTACT G. D. Malkasian, Jr., M.D., Dept. of Ob/Gyn, Mayo Clinic, Rochester, MN 55901, 507/284-2511.

**Slow Viruses, Chronic Disease and Autoimmunity**; U of M-Duluth School of Medicine; UMD; Sept. 26-27; CONTACT Lynn Devlin, UMD School of Medicine, 2400 Oakland Ave., Duluth, MN 55812, 218/726-7581.

### October, 1980

**Internal Medicine Review**; U of M Medical School; U of M Mpls.; Oct. 1-3; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Enhancing Your Financial Skills**; MMA, Hennepin County Medical Society, Ramsey County Medical Society; Decathlon Club, Mpls.; Oct. 9; CONTACT Dave Luth, MMA, Suite 900 American National Bank Bldg., St. Paul, MN 55101, 612/222-6366. (Management seminars will also be held on Oct. 7, 8, & 10 for medical office personnel.)

**Third Annual CNS Disease Symposium**; U of M Medical School with Hennepin County Medical Ctr.; Hennepin Co. Medical Ctr., Mpls.; Oct. 10; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Pediatric Seminar**; Minneapolis Children's Health Center and St. Paul Children's Hospital; Mpls. Children's Health Ctr., Mpls.; Oct. 10; CONTACT Daniel P. Kohen, M.D., 2525 Chicago Ave. So., Mpls., MN 55404, 612/874-6238.

Joint Meeting, **MN Society of Internal Medicine & MN Chapter, American College of Physicians**; St. Paul-Ramsey Med. Ctr.; Oct. 10; CONTACT Brian Campion, M.D., St. Paul-Ramsey Med. Ctr., 640 Jackson St., St. Paul, MN 55101, 612/221-3456 and Josesh Cardamone, M.D., Mercy Medical Center, 4050 Coon Rapids Blvd., Coon Rapids, MN 55433, 612/427-2200 Ext. 2367.



## CME IN MINNESOTA

### October (Continued)

- 4th Annual Current Concepts in Ophthalmology;** Mount Sinai Hospital; L'hotel de France, Mpls.; Oct. 11; CONTACT Mrs. Evelyn Peterson, Medical Staff Secretary, Mount Sinai Hospital, 2215 Park Ave., Mpls., MN 55404, 612/871-3700, ext. 1117.
- Neonatology;** Central Mesabi Medical Center; CMMC; Oct. 13; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.
- Annual Ob/Gyn Autumn Seminar;** U of M Medical School; Mayo Memorial Auditorium, Mpls.; Oct. 15-17; CONTACT CME Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Electrical Pacing in Diagnosis and Treatment of Cardiac Arrhythmias;** U of M Medical School; U of M Mpls.; Oct. 16-17; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Basic Cardiac Life Support Instructor Course;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Oct. 20-21; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.
- Cardiovascular Disease Conference with Clinical Preceptorship;** U of M Medical School; St. Paul Ramsey Medical Center; Oct. 23-25; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Seminar for Directors of Medical Education;** MMA; Spring Hill Center, Wayzata; Oct. 24-26; CONTACT Teresa L. Rogstad, Suite 900 American National Bank Bldg., St. Paul, MN 55101, 612/222-6366.
- Poisoning: A Brief Symposium;** U of M Medical School; St. Paul Ramsey Medical Center; Oct. 24; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- ENT for Primary Care Physicians;** Mayo Foundation; Mayo Clinic, Rochester; Oct. 26; CONTACT Postgraduate Courses, Rm. 720, Plummer Bldg., Mayo Clinic, Mayo Foundation, Rochester, MN 55901, 507/284-2085.
- Clinical Reviews;** Mayo Foundation; Mayo Clinic, Rochester; Oct. 27-29; Nov. 10-12; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.
- Principles of Colon & Rectal Surgery;** U of M Medical School; U of M Mpls.; Oct. 29-Nov. 1; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### November, 1980

- Fall Scientific Program; MN Society of Anesthesiologists;** L'hotel de France, Mpls.; Nov. 1; CONTACT David Byer, M.D., 2001 1st St. S.W., Rochester, MN 55901, 507/286-8701.
- Workshop on Heart Attack Prevention;** U of M Medical School; Spring Hill Center, Wayzata; Nov. 4-6; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Neonatal Resuscitation;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 6; CONTACT Mark Bixby, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.
- Current Topics in Pulmonary Pathology;** U of M Medical School; U of M Mpls.; Nov. 6-7; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Update in Oncology for Primary Care Physicians;** American Cancer Society, MN Div. Inc.; Radisson Hotel, St. Paul; Nov. 7; CONTACT Caryl Range, 2750 Park Ave., Mpls., MN 55407, 612/871-2111.
- Advanced Cardiac Life Support Course;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 7-8; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.
- Update in Cardiology;** Mayo Foundation; Mayo Clinic, Rochester; Nov. 9; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.
- Ophthalmology for Primary Care;** U of M Medical School; Sheraton Ritz Hotel, Mpls.; Nov. 14-15; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Practical Therapy of Malignant Disease;** Duluth Clinic LTD.; St. Mary's Hospital, Duluth; Nov. 15; CONTACT J. G. Brueggemann, M.D., Dir. of Medical Education, Duluth Clinic, LTD., 400 E. 3rd St., Duluth, MN 55805, 218/722-8364.
- Endocrinology;** Central Mesabi Medical Center; CMMC; Nov. 19; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.
- Nordic Sports: A Scientific Approach;** U of M Medical School; Mt. Telemark, WI; Nov. 20-23; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### December, 1980

- Thirteenth OB-GYN Symposium;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Dec. 5; CONTACT Milton Baker, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.
- Winter Meeting, MN Obstetrical & Gynecological Society;** North Memorial Medical Center, Mpls.; Dec. 6; CONTACT Richard Bendel, M.D., Hennepin County Medical Center, 701 Park Ave. S., Mpls., 55415, 612/347-2750.
- New Concepts of Otolological Surgery and Clinical Problems in Otitis Media;** U of M Medical School with Lions International Hearing Center-Mpls., Chilean Medical Association, Chilean Society of Otolaryngology; Carrera Hotel, Santiago, Chile; Dec. 11-13; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.
- Oncology;** Central Mesabi Medical Center; CMMC, Hibbing; Dec. 16; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.

### January, 1980

- Winter Seminar; MN Academy of Family Physicians;** Puerta Vallarta, Mexico; Jan. 16-26; CONTACT Chari Konerza, Exec. Dir., MAFP, 8455 Flying Cloud Drive, Eden Prairie, MN 55344, 612/944-3585.

For further information on the above or future CME programs, contact Teresa L. Rogstad, Director, Department of CME & Program Services, Minnesota Medical Association, Suite 900, American National Bank Building, 101 East 5th Street, St. Paul, Minnesota 55101 (612/222-6366).



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# President's Letter



## Frank E. Johnson, M.D.

Frank Johnson appeared like a meteor in the councils of the Minnesota Medical Association in 1978. He had been relatively uninvolved in the activities of our Association before that time, although he was a recent President and Chairman of the Board of the Hennepin County Medical Society. In that organization he acquired the sobriquet of "Mr. Yesterday", because when a good new idea was brought forth, he was always puzzled why it had not already been adopted and implemented.

Early in his year as president-elect, Frank expressed to me his concern that one year as President of the Minnesota Medical Association would not be enough time for him to do those things that he felt should be done. His record gives lie to that concern.

Frank was a principal architect in the development of the Minnesota Medical Insurance Exchange, a physician-owned liability carrier developed by the Minnesota Medical Association for its members.

Frank was the driving force in the activities which led to the planning and construction of the Health Associations Center on University Avenue. It is appropriate that Frank Johnson's contributions be recognized in the October, 1980, issue of MINNESOTA MEDICINE, because it is in this month that the Minnesota Medical Association will move into that building.

Frank has made other major contributions to this Association. He is still searching for ways to aid its growth and improve its function. In particular, he would like to find ways that the Association might develop activities for profit which might reduce the pressure on dues dollars.

The Minnesota Medical Association will reap the benefits of his distinguished service for a long time to come.

A handwritten signature in cursive script that reads "John K. Meinert M.D.".

John K. Meinert, M.D.  
President  
Minnesota Medical Association



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# Editor's Notebook

## A Chinaman's Chance Impressions of China and Chinese Medicine

*"China? There lies a sleeping giant. Let him sleep! For when he wakes he will move the world."*

*Napoleon*

*"China has stood up."*

*Mao Tse-Tung, 1949*

*"China wants to catch up with the West and to do it quickly."*

*Tsung Cheng, M.D.*

*Annals of Internal Medicine*

I shall begin with three semi-apologies:

1. This essay rests on what I observed during two weeks in China. Our tour covered Canton, Shanghai, Shenyang, and Peking. Since China is big (it is slightly larger than the United States), old (it has more than 4000 years of continuous civilization), complex (55 ethnic groups comprise its one billion people), subtle (the Chinese say yes when they mean no), and contradictory (they are polite people yet have a history of uninterrupted violence), I will only be scratching the surface. If you dig too deep, you reach the United States anyway. To make matters even more superficial, the Chinese control where you go, show you only what they want you to see, and segregate you from the populace when you are eating, sleeping, or shopping. Still, the Chinese have a knack for making the most controlled and staged events appear spontaneous.

2. I have taken the liberty of being light about a deadly serious subject. China is essentially a humorless place, at least to this roving American eye. The Chinese are earnest, hardworking, and purposeful. Their favorite comedian is Charlie Chaplin, and they savor him because they regard his films, especially the *Time Machine*, as savage satires on American capitalism. I don't mean to imply the Chinese are oppressed, unsmiling, sullen, or unhappy. They are not. They are simply terribly serious, utterly convinced of the superiority of their culture over any other. This attitude does not lend itself to humor.

3. I have chosen the masculine gender in the title, in my opening three quotes, and in the text. For this, I will be hearing from feminists about my male chauvinism. But I find it more comfortable to say "he" and "she" rather than "person". Besides, "Chairperson Mao" doesn't strike me right. Even if some of my readers do not forgive me for perpetrating this anachronistic habit of the past, God will. *She* will forgive me. As an afterthought, I should add Chinese women were given complete equality in 1950, in keeping with the spirit of the "liberation" (translate "liberation" in English to "conquest" of the Nationalist forces).

### Impressions of China

Now, for my impressions. I shall go straight to the point: China is a feast for the senses — sight, smell, taste, and feel.

Visually, the masses of people are overwhelming. Everywhere you see people, in the streets, on the rooftops, behind the walls, and coming out of the woodwork. It seems you can't stand anywhere and throw a rock without hitting a Chinaman. As your train (Japanese and air-conditioned) rolls through the countryside,



you witness a stream of contiguous villages. Immediately you sense the contrast between the Chinese and American countrysides and these reasons why. China is about 85 percent statistical rural; the United States is 25 percent. In China, it takes 75 to 80 percent of the people to work the land; in America five to seven percent do the job. In America where you would see a farmhouse, in China you see a village. In America, one farmer on one tractor tills a field; in China, fifty to 100 workers stand, stoop, or toil among the furrows or paddies in the same sized field.

Bicycles clog the highways and byways. Consequently, for the tourist, bus travel is a prolonged exercise in continuous hornblowing, with wave upon wave of bicycles parting in front of you. The foot traffic poses more of a congestion problem than the bicycle jams. Bicycles you see, cost \$90 to \$100 in a society in which the average worker brings home less than \$50 a month. The State forbids private cars. Because of heavy foot traffic, grass and lawns, as we know them, are absent. In most public places, in grounds around buildings, on shoulders of the road, and on river and canal banks, bare earth shows.

Finally, there is the visual monotony of cars, trucks, dress, and building. The universal car is the Shanghai, which is a dead ringer for a 1950 Plymouth and comes in one color, black; most trucks are khaki and resemble left-overs from World War II; the universal garb is white shirts or blouses, untucked at the waist, loose-fitting dark trousers, slacks, or shorts and either opened toed sandals or closed canvas or leather work shoes; and the characteristic housing is a high-rise tenement — plain, unpainted, either concrete slab or brick, and “functional.” By functional, I mean, is nothing that will please the eye, stir the heart, or spark the spirit.

Smell? Well, try this out on your nose: China has little central sewage, maintains communal outhouses for most citizens, recycles all human excrement for fertilizer use, markets few perfumes or deodorants, burns lowgrade coal to heat homes and public buildings and to generate electricity, and maintains no pollution controls for low-grade gas or diesel-consuming trucks and buses. In Shanghai alone, workers haul out 10,000 tons of night soil each morning for later use in the fields around that city of 12 million. This night soil is held in cement vats for ten days before being used as fertilizer. The holding process lessens the odor. Thanks to the saving grace of that physiological phenomenon known as olfactory fatigue, the smells mercifully diminish after a few days.

Taste of food? Among our group of 22, opinions varied, but most of us enjoyed our meals. The typical table setting includes a small plate, a tea cup, chopsticks, three glasses (beer, wine, and *maoti*, which goes down like 140 proof diesel fuel), and the Chinese equivalent of kleenex (which substitutes for napkins). You receive eight to ten dishes, which arrive one at a time, and vary from crisp to tender, to dry and heavily spiced. Soup and rice are invariably served, and you will be offered things you never considered edible but are. The vegetables are fresh, varied, and sometimes unrecognizable. Much of the meat, especially the fish, is suspect. The Chinese do not debone anything (fragments of bone and marrow, it is said, diffuse into the meat, flavoring it and supplying essential minerals), so you must pick your way carefully. We did not, to our knowledge, have any “hornless goat”, i.e. dog, but we experienced excellent Peking duck, served with bean curd and raw green onions and wrapped in a flat pancake. You will not starve in China. If anything, you are served too much.

By the sense of “feel”, I mean the ambience — the pervasive atmosphere — of the people, the politics, and the place. The people make a vivid impression. They work hard, exercise diligently, look clean and fit, are polite and modest, get along harmoniously, and follow the rules. Furthermore, they are exceedingly moral. If you believe your hosts and your limited observations, they do not steal, drink excessively, take drugs, fornicate out of wedlock, prevaricate, accept tips, nor have selfish thoughts. Many of these paragons of virtue do, however, smoke like chimneys and somehow, through some sexual legerdemain, have produced 600 million people in the last 30 years. Say what you will about Chinese communism, you have to grant what Mao and his followers accomplished: restored the work ethic, achieved a cohesive morality, and instilled into the Chinese a sense of pride — in themselves, their culture, their past, and their future.



In my opinion, the Chinese have a genuine affinity and affection for Americans. Just why, I'm not sure, but, our guide told us we were, more "open" than other foreigners. Indeed, our guide observed that while the British think before they talk; the Americans talk before they think. We took this as a compliment.

The children are particularly friendly, smiling at you, clapping when you arrive and depart, and even dancing with you. The Chinese, adults and children alike, marvel at Polaroid cameras. Take a picture and you create an instant crowd, which develops rapidly. Parents thrust children in front of you to be photographed. In my case, I ended up giving away most of my Polaroid pictures.

The Chinese often gawk at you, as if you were from Mars. This is understandable when you realize these people have been isolated for thirty years. Indeed, sixty percent have been born since 1949. Small wonder, then, that many Chinese gape with startled curiosity at these strange beings with white skin, blond hair, blue eyes, jewelry, colorful clothes, and painted faces, fingernails, and toenails.

Before departing from the people, a note about T'ai chi. This is a slow-moving, rhythmic and meditative exercise that all ages practice each morning. "Mass participation" is one of the keystones of the Chinese Communist philosophy, and nowhere is it more apparent or more effectively demonstrated than in the streets and parks where millions of Chinese perform this oriental exercise. Rather than describe T'ai chi myself, I will quote this recent descriptive passage from the *New York Times*.<sup>1</sup>

"Developed centuries ago, t'ai chi is among the earliest of the Oriental martial arts. But while forms such as Chinese kung-fu and Japanese karate are combat-oriented, emphasizing swiftly delivered blows and kicks, t'ai chi does not require a combatant. It is flowing and slow-moving; the kicks and punches have become abstracted so that it's closer to a slow-motion dance than to a Bruce Lee action sequence.

T'ai chi is performed standing, following a set pattern of restrained movement that emanates from the *tan'ien*, or center of gravity. Depending on the form followed, the sequence of movement can take between ten and 50 minutes. Practiced in China by people of all ages, t'ai chi is not regarded principally as a means of self-defense but as a gentle form of exercise and as a calming meditation.

Legend has it that t'ai chi originated early in the 14th century when a monk, sitting in meditation in his garden, observed a shrike attacking a snake. Each time the bird swooped down on the snake, the reptile eluded its attacker through flowing, sinuous movements. The monk, enlightened by watching this example of brute force overcome by gentle yield, created the t'ai chi dance upon the spot."

After that little exercise, I dare say I have worked my proposition off on you that the Chinese are a distinctly different people.

This is true of politics, as well as exercise. In politics, you do not feel the heavy-handed repression or surveillance you sense in Russia or the Eastern Bloc countries. It is wise to keep in mind that the Chinese and Russian brands of Communism evolved differently: Lenin's came out of the cities, where the industrial workers formed the core of the movement; Mao's rose out of the countryside, where the intellectuals mobilized the peasants. Chinese Communism is more paternalistic towards its people, and perhaps it can afford to be. The Chinese, after all, naturally worship the group, rather than the individual. Also, because of the high population density and the lack of mobility — educationally, socially, or by mechanized means — the Chinese are relatively trapped in their communities. In China's seamless society, it is difficult for an individual who thinks independently to create mischief. Finally, the Communist leaders keep their lines of communication, the so-called "mass line", open to the peasants. The leaders, in short, know and satisfy their constituency. Still, the Communist government maintains a bloated and rigid bureaucracy, complete with banners and slogans.

Just a word, if I may, about the slogans and banners. You could always spot the banners — roughly two feet high and six feet long, red, cloth, with a string of Chinese characters culminating in an exclamation point. At the Friendship Stores, where Americans and other foreigners shop, the banners are bigger and in English. Most contain Mao's sayings, such as "Unite, and struggle for building up a modernized and powerful



socialized country!" Mao, incidently, has been demoted by the Party from a demi-god to merely a great man. According to the Premier, Hua Guofung who was peacefully replaced during our visit, Mao was "70 percent right and 30 percent wrong", with most of his mistakes being attributed to his senescence and the Gang of Four — Mao's widow and three others from Shanghai — who supposedly influenced him during his last stages and seized power after his death. I tried to obtain a copy of Mao's little red book, the "Quotations from Chairman Mao Tse-Tung" but was informed that the book was "finished" because Mao had made "mistakes."

The slogans, and the rewriting of history struck an Orwellian chord in my mind. George Orwell, if you'll remember, wrote a book in 1946 called "1984". Its chief character, Winston Smith, worked in the Ministry of Truth, where his job was to continually rewrite the past to fit the current political situation. The official language of Smith's totalitarian country, Oceania, was called Newspeak and consisted of lying and deceit for political purposes. The government, as in China, was outwardly paternalistic but inwardly repressive, and it had three slogans:

"WAR IS PEACE"  
"FREEDOM IS SLAVERY"  
"IGNORANCE IS STRENGTH"

It is easy to overdo the analogies, for Orwell was writing about English Socialism, but the Chinese government does the same kind of things that Oceania did — it politicizes everything, it controls channels of thought, it remolds news and history to match current policies, it regulates privacy, it eliminates eroticism, and it practices GroupThink. The Party, in short, is the Guardian of Truth. By tradition, by necessity, and by choice, the Chinese work in groups anyway.

The Chinese seem to follow the gist of Oceania's slogans: (1) WAR IS PEACE. With the Chinese, there is always a "struggle" against some imagined internal or external adversary — past emperors and landlords, China Kai-shek, intellectuals in general, the Gang of Four in particular, and Russia. These "struggles" are a propaganda weapon to whip up the moral of the people; (2) FREEDOM IS SLAVERY. The Chinese equivalent of FREEDOM is individualism, which, according to the Chinese lures people into thinking capitalism is good when it is really enslaving. In Shenyang, we learned, for example, that the Chinese promote this view of the American housewife. She is a power hungry individualist, who does not rouse until 10 in the morning, and then only to be fed by her enslaved husband, who must bring home the material goods demanded by his wife, who thinks only of herself, rather than her family; and (3) IGNORANCE IS STRENGTH. To the Chinese Communists, the intellectuals have always been viewed with suspicion. They are untrustworthy, because: (a) they come from capitalist backgrounds; (b) they have no compassion for the peasants; (c) they work with their minds, rather than their hands; and (d) most heinous of all, they are individuals who seek to better themselves and separate themselves from the masses. This set of attitudes contributed heavily to the Cultural Revolution, which started in 1966, and which from 1966 to 1976 closed most Chinese Universities and medical schools. In any event, the underlying IGNORANCE IS STRENGTH philosophy of the party and people led to public assaults on teachers, scientists, and physicians; to forced confessions for deviant political thinking; and to removal to rural areas of intellectuals for forced menial labor and for "reeducation". As might be suspected, the Cultural Revolution left gaping holes in Chinese intellectual circles, including the medical communities and set back economic progress and research for years. As a consequence of this generation gap in medical education, most medical schools had 70 and 80-year -old professors.

### Impressions of Chinese Medicine

I have saved this for last because Chinese Medicine must be considered in the context of Chinese culture. In talking about this subject, I want to establish three points:

1. By common consensus, the Chinese government has done a magnificent job in Public Health. Although health statistics are limited, countless visitors to China have attested the vigorous good health of the people.



Through the fostering of mass participation campaigns, China has brought infectious diseases under control, drastically reduced the incidence of venereal disease, and provided most citizens with good diets, adequate sanitation, safe water supplies, and suitable food and shelter. For the first time in recorded history, the great masses of Chinese have a chance for good health and a long and secure life. The old phrase, "not a Chinaman's chance", no longer applies. The average Chinaman has hope, and that is remarkable in a country where malnutrition, infectious disease, and infant deaths were once rampant.

2. Chinese disease and mortality statistics are spotty at best, and sources of semi-scientific information, such as the *Chinese Medical Journal*, are often too politicized to draw any hard and fast conclusions about the quality of Chinese medicine.

3. The efficacy of Chinese "traditional" medicine, which has existed for 2000 years and which employs large doses of inscrutable philosophy, thousands of herbs, millions of acupuncture needles, and strange mixtures of therapies, such as moxibustion and mustard plasters, are simply too much for the biased Western scientific mind to handle or judge.

I shall, therefore, restrict myself to what I saw, heard, or recorded in my diary. We visited three medical establishments: a 650 bed "Western" hospital in Shanghai for railroad workers, a 500 bed "combined" hospital, in Shenyang where 1800 staff members not only treated patients, but taught traditional and western medicine to 1500 medical students; and a small commune clinic in a village, just outside Shenyang. This is a limited exposure. China has 117 medical schools with 30,000 students, 64,000 hospitals, with 1.85 million beds, and this distribution of vocational manpower in the health care:<sup>2</sup>

**Table 1. Manpower Distribution Among the Vocational Fields of Health Care in China<sup>2</sup>**

<b>Western doctors</b>	<b>358 520</b>
<b>Traditional doctors</b>	<b>251 088</b>
<b>Pharmacists</b>	<b>16 749</b>
<b>Herbalists</b>	<b>94 854</b>
<b>Technicians</b>	<b>8447</b>
<b>Middle doctors</b>	<b>423 410</b>
<b>Nurses</b>	<b>406 649</b>
<b>Midwives</b>	<b>70 555</b>
<b>Barefoot doctors</b>	<b>1 600 000</b>
<b>Paramedical personnel</b>	<b>800 000</b>
<b>Total health manpower in 1978</b>	<b>4 030 272</b>

There are two basic approaches to describe Chinese medicine: (1) to compare in glowing terms the present situation to pre-liberation days before 1949; (2) to compare unfavorably present conditions to those existing in the West. Neither approach lends itself to objectivity, but I have leaned towards the second since I have no other base for comparison.

Here, briefly, from fleeting exposures, is what I saw and concluded in my diary.

"August 29, 1980, Shanghai. Spent two hours at 650 bed railroad hospital. My impressions? (1) primitive by American standards; (2) a hospital is a place for those Chinese patients unable to care for themselves; (3) inadequately financed by central government; (4) old, most facilities at least 50 years old; (5) medical staff — reasonably competent and doing their best but starved for information.

"My basis for these conclusions are a visit to a medical ward, observation of thyroid adenoma removal under acupuncture anesthesia; and a free-ranging 30-minute discussion with five medical staff members. Doctors are abnormally paid, about \$60 to \$90 a month, but that is more than factory workers at \$20 to \$40 a month. With hospital rooms costing \$1.00 a day, operations \$6 to \$30, and housing rent \$10 to \$20 a month, maybe doctors' pay isn't bad. I don't really buy that, though, because I believe professional and managerial classes, outside the party are repressed here."



Just a few comments in the acupuncture anesthesia. We observed a partial thyroidectomy on a 50-year-old male. He had a known thyroid nodule for two years. Twenty minutes before the start of surgery, two acupuncture needles were inserted into the web of each thumb and into the back of the hand. He was given luminal preoperatively, but no intravenous fluid was running during surgery. When we arrived, the patient's hands were twitching spasmodically, because the acupuncture needles were attached to a low voltage stimulator. The only person wearing sterile gloves was the surgeon. At the opening incision, and during the early dissection, the patient grimaced and winced but did not utter a sound. The procedure went smoothly. The surgeon looked skillful and took 30 minutes to remove a benign thyroid adenoma.

From the Chinese Medical Hospital in Shenyang, I recorded these notes:

"Visited Hospital of Traditional Chinese Medicine. We were informed hospital was founded in 1958, during the Great Leap Forward. Government is now stressing combined approach — traditional and Western Medicine. Mao emphasized traditional medicine. In his memory, government decided to initiate combined curriculum, which will start next year and will take seven years to complete.

"Toured treatment rooms and saw the following: (1) carious teeth being removed after a few minutes of digital pressure on trigeminal and lingual nerves. One of our fellow travelers, a dentist from Buffalo, New York, noted that patients had pyorrhea and that roots were left behind; (2) chronic tonsillitis being treated by cautery. Medical assistants dipped metal instruments into sesame oil, flamed them, then cauterized tonsils of sitting patients who had received no local anesthetic; (3) patients with numerous ailments — rheumatoid arthritis, neuroses, Bell's palsy, cerebral palsy, bursitis and stroke palsies — being treated with multiple acupuncture needles; (4) a group of patients undergoing a variety of moxibustion treatments. Moxibustion is burning of herbs to raise blisters over certain points of body. Acupuncture and moxibustion are both based on complex theoretical system of meridians running over surface of body and covering hundreds of points related to internal and external functions, and (5) a spotless painted room (the only such room I saw in a Chinese hospital or clinic) for displaying specimens for teaching students. These specimens included ginger root, antelope horns, seahorses, snakes, stuffed animals, minerals, and a variety of medicinal herbs."

### Concluding Remarks

Since 1949, China's medical achievements have been in the fields of preventive medicine, public health, and health care reorganization. In medical technology, China lags far behind the West. No head or body scanners exist in China, and there is only one SMA-12/60. It sits in Peking and runs only on the BUN channel. In research, China talks of developing a male oral contraceptive, using serum alpha-fetoprotein to detect liver cancer, doing a few renal transplants, making minor advances in cardiac surgery, treating total body burns with success, and reimplanting severed limbs and reconstructing thumbs and fingers from transplanted toes. But the scope of these developments are minor when matched against those of the West. Perhaps China's most stunning achievement is effective birth control. During our visit, Peking radio announced China's birth rate had plummeted from 95,000 to 47,000 a day in ten years. That bodes well for China. After all, the fewer Chinamen, the greater the Chinaman's chance.

*Richard L. Reece MD*

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# Stat Tonsillectomy for Peritonsillar Abscess

JOSEPH H. LEEK, M.D.\*

Three methods of medical care, singly or in combination, to treat an acute abscess in the peritonsillar space are discussed.

THREE METHODS of medical care, singly or in combination, are available to treat an acute abscess in the peritonsillar space: (1) Use of medications and time; (2) Incision and drainage of the localized abscess and (3) Tonsillectomy during the acute phase on a semi-emergency basis.

I will briefly discuss the first two methods and then elaborate on and recommend the third method.

### Method 1

The morbidity associated with acute peritonsillar abscess is usually profound and requires medical care. Bacteria, usually beta streptococcus Group A, account for the majority of infections. Appropriate throat and occasionally blood cultures should be a prerequisite to starting antibiotic medications. Intravenous fluids frequently will be needed when trismus and dysphagia restrict adequate fluid intake in more severe cases.

Although the infection can be controlled and the abscess sterilized using antibiotics, only spontaneous rupture assures evacuation of the enclosed empyema. The risks of the abscess dissecting into the retropharyngeal space or sudden rupture into the pharynx with potential tracheal aspiration create concern for the patient until the acute illness is controlled. Those cases treated in this conservative way have a probability of recurring tonsil infections with or without abscesses.

### Method 2

Surgical dogma has steadfastly stated that incision and drainage is mandatory for a known abscess. When a peritonsillar abscess points, surgical evacuation usually brings prompt relief from the morbidity and often rapid resolution of the illness. Unfortunately, only 70% of the abscesses will localize near the upper pole where incision and drainage are convenient.<sup>1</sup> The remaining 30% will be in the mid or lower portion of the tonsil fossa making incision and drainage more difficult. The drainage wound to the abscess space should be probed daily until it is dry.

The literature suggests that an elective tonsillectomy should be considered four to six weeks after the acute

infection is resolved.<sup>2</sup> Tonsillectomy can be difficult after an abscess occurs. The usual cleavage planes often are obliterated requiring sharp dissection techniques. The tonsil capsule and fossa wall integrity can be compromised and bleeding more significant.

### Method 3

Tonsillectomy to treat a peritonsillar abscess was first documented in 1859.<sup>3</sup> This method then became popular in Europe but did not gain favor in this country. The objection seemed to relate to the possibility of septicemia. I suspect also that the technical difficulties inherent in doing this procedure using local anesthesia deterred many surgeons in the past. Preoperative systemic antibiotic therapy and general anesthesia employing an endotracheal system reduces both these objections.

In February, 1977, I did my first tonsillectomy to treat an acute peritonsillar abscess. During the same surgical procedure the opposite tonsil was removed. Subsequently 15 tonsillectomies have been done by me for this same disease (Table 1).

TABLE 1		
Demography		
Numbers	Years of Age	Median
15	8-39	21
12	17-20	18.5

The patients were hospitalized 0-4 days before surgery was performed. In several patients an immediate diagnosis was delayed, the illness most commonly being confused with infectious mononucleosis. When the diagnosis became obvious, surgery was performed on a semi-urgent basis. In this group of patients none of the abscesses spontaneously ruptured and none resolved medically, albeit surgery was done before either of these conditions might have occurred.

Surgery was done in the operating suite under controlled conditions. All the patients received general anesthesia with endotracheal intubation. No local anesthetic or adrenalin was used. The abscessed tonsil was removed first and then the other tonsil was electively taken out. After the basic pillar incisions

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were made and the tonsil dome exposed, the abscessed space was entered and frequently the tonsil fell free of the fossa, the abscess having done the bulk of the dissection. Bleeding was usually minimal and the maximum estimated blood loss in any of these patients was 100 ccs. Control of bleeding was remarkably easy requiring only pressure or infrequent cautery (Table 2).

TABLE 2

Amount	No. of Patients
50 cc.	1
50-100 cc.	13
100 cc.	1

The opposite tonsil usually behaved like any routine adult procedure. Interestingly, three cases had small abscesses on the silent side. Bleeding tended to be more significant on this side.

Following surgery, these patients did well. There were no postoperative hemorrhages and none had increased toxicity. The majority left the hospital one or two days after surgery with only two staying for three days (Table 3).

TABLE 3

	Days of Hospitalization	Median
Preoperative	0-4	1.3
Post operative	1-3	1.7
Total	1-6	3.0

### Summary

Although an abscess in the peritonsillar space might subside spontaneously or clear completely with antibiotic therapy, the majority will require some drainage procedure. If this is needed I recommend that a primary tonsillectomy be done in lieu of incision and drainage and the interval tonsillectomy. There does not appear to be an increased risk. The goal of drainage is more effectively accomplished and there is assurance that further difficulty with tonsil disease is ended. Total hospital care, both primarily and for future need, will probably be shorter. This reduced utilization should be cost effective.

I suggest you try this method of care for your next peritonsillar abscess; I think you will agree.

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# Impotence

## Pathogenesis and Evaluation

ARTHUR D. SMITH, M.D.\* and PAUL H. LANGE, M.D.†

It has long been recognized that a major cause of impotence is psychological disturbances, but recently newer methods of evaluation have revealed that organic causes are much more common than previously appreciated. Many of the organic causes of impotence are enumerated in this article but two of the most common, and heretofore often overlooked, are occult occlusive-vascular and neurologic diseases. Identification of the causes of impotence is becoming increasingly important, not only because the correct surgical or psychological treatments in properly diagnosed patients are highly successful, but also because third-party medical payment organizations provide financial assistance to the patient only if his impotence is clearly proven to have an organic cause. Thorough evaluation with a variety of laboratory and clinical tools is often necessary in impotent patients to define the underlying causes and best treatments.

**I**MPOTENCE, OR ERECTILE dysfunction, is the persistent inability to obtain or sustain an erection that is sufficient to allow intromission, pelvic thrusting and, in the absence of ejaculatory difficulties, ejaculation during sexual intercourse.<sup>1</sup> It is important to define impotence precisely, distinguishing between it and other male sexual dysfunctions such as premature ejaculation, retarded ejaculation, and loss of libido. In fact, loss of erectile function is often present in men who still have normal libido, orgasm, and sometimes ejaculatory function. The man with primary erectile dysfunction has never been able to perform sexually, whereas the man with secondary impotence previously had normal sexual function which has become impaired.

In 1959 Wershub<sup>2</sup> stated that 90% of impotence was psychogenic and only 10% due to organic causes. With more extensive evaluation, however, it is becoming apparent that organic impotence is more prevalent than was previously realized, and its true incidence is probably in excess of 50%.

### Physiology of Erection

The blood supply of the penis is via the internal

pudendal artery, a branch of the hypogastric artery. The internal pudendal artery divides into three terminal branches: the deep penile artery supplying the corpora cavernosa, the dorsal artery of the penis which lies deep to Buck's fascia, and the artery of the bulb. The deep penile and dorsal branches anastomose around the corona of the glans and communicate throughout their course via penetrating branches, while the artery of the bulb supplies the corpus spongiosum.

The cavernous erectile tissue of the penis can be compared to a sponge with an arterial inflow and venous outflow. Tumescence occurs when the sponge is full and regulation of the mechanism is dependent on the inflow and outflow of the blood. Conti<sup>3</sup> initially described the presence of small muscular pillars called polsters situated in the arterioles and venules supplying the corpora cavernosa. Erection is achieved by a contraction of the venous polsters and relaxation of the arterial polsters. Recently, Benson<sup>4</sup> was unable to demonstrate<sup>5</sup> these polsters and ascribes the mechanism of erection to a variable degree of vasodilatation.

It is postulated that there are two centers for neurologic erection: one in the sacral cord (S2 through S4) and the other in the thoracolumbar cord (T12, L1). Tumescence may result from cortical stimuli (olfactory, auditory, fantasy, and the like), producing what is known as psychogenic erection. This is thought to be mediated via the thoracolumbar outflow and the

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hypogastric plexus. Local stimulation of the penis also results in tumescence, which is called reflexogenic erection. The pathways responsible for reflexogenic erections are the afferent nerve supply of the penis via the pudendal nerve, and the efferent supply via parasympathetic fibers S2 and S4 carried in the nervi erigentes. This pathway is responsible for reflexogenic erections. In normal circumstances, both the sympathetic fibers from the thoracolumbar outflow and the nervi erigentes probably influence the vascular mechanism responsible for tumescence.

### Causes of Impotence

#### Psychological

Masters and Johnson<sup>5</sup> found the following to be the major psychological causes of impotence: (1) following premature ejaculation, (2) alcohol intake, (3) maternal or paternal dominance, (4) religious orthodoxy, (5) homosexuality, (6) personal devaluation,

and (7) marital disharmony. Often a combination of these psychological factors exists, and there may also be an organic basis for the condition. For these reasons, the situation may be extremely complex and the evaluation must therefore be thorough.

#### Organic

There are many causes of organic impotence. The following simple mnemonic may be helpful in bringing the causes for impotence to mind: inflammatory, mechanical, postoperative, occlusive-vascular, traumatic, endurance, neurologic, chemical, and endocrine. A listing of examples of these divisions may be seen in Table 1.

Although a local inflammatory reaction may result in a reflex erection, temporary impotence is a more common result, especially with acute lesions such as acute urethritis or acute cystitis. Successful treatment of these conditions often cures the impotence.

The mechanical causes of impotence are usually

TABLE 1  
Organic Causes for Impotence

<b>Inflammatory</b>	<b>Neurologic</b>
Urethritis	Electrical shock therapy
Prostatitis	Temporal lobe lesions
Seminal vesiculitis	Parkinsonism
Cystitis	Head injuries
Urethral stricture	Cord tumors or transections
Gonorrhea	Amyotrophic lateral sclerosis
Nonspecific infections	Multiple sclerosis
Tuberculosis	Spina bifida
<b>Mechanical</b>	Syringomyelia
Congenital deformities (exstrophy, epispadias, hypospadias, chordee, microphallus)	Subacute combined degeneration of cord
Peyronie's disease	Tabes dorsalis
Morbid obesity	Peripheral neuropathies
Large hydrocele	<b>Chemical</b>
Phimosis	Drugs of addiction (alcohol, amphetamines, barbiturates, bromides, opiates)
<b>Postoperative</b>	Drugs used in psychiatry (benzodiazepines, phenothiazines, thioxanthenes, tricyclic antidepressants, MAO inhibitors)
Perineal prostatic biopsies	Drugs used in neurology (antiepileptics, antiparkinson)
Simple prostatectomy	Drugs used in cardiology (clonidine, digoxin, methyldopa, phenoxybenzamine, propranolol, <i>Rauwolfia</i> derivatives, spironolactone, thiazides)
Radical prostatocystectomy	Other drugs (anticholinergics, ganglion blocking drugs, immunosuppressives, cimetidine)
Abdominoperineal resection	<b>Endocrine</b>
Vascular surgery	Pituitary (acromegaly, chromophobe adenoma, craniopharyngioma, pituitary ablation)
External sphincterotomy	Adrenal (neoplasm with or without Cushing's or Addison's syndrome)
<b>Occlusive-vascular</b>	Thyroid (myxedema, thyrotoxicosis)
Large vessel disease (atherosclerosis)	Gonadal (castration or past inflammatory fibrosis; exogenous estrogens; Klinefelter's, Reifenstein's, and male Turner's syndromes; feminizing testicular tumors)
Small vessel disease (arteritis, priapism)	Pancreatic (diabetes mellitus)
Thrombosis and embolic phenomena	
<b>Trauma</b>	
Penectomy (surgical or traumatic)	
Ruptured urethra	
<b>Endurance</b>	
Myocardial failure (acute or chronic)	
Pulmonary insufficiency (acute or chronic)	
Anemias and leukemias	
Systemic illnesses (infections, nutritional, immunologic)	
Metabolic disease (renal and hepatic failure)	



obvious. Peyronie's disease causes impotence if there is associated severe pain or marked deformity of the penis caused by the fibrotic plaques. Impotence in Peyronie's disease may also occur as a complication of its treatment either by surgery or irradiation. Phimosis causes local pain and may, therefore, inhibit erection. One of the best publicly documented cases of impotence due to phimosis is that of Louis XVI who was King of France from 1775 to 1789. For the first seven years of marriage, the young king is believed to have been totally impotent and the marriage was not consummated. Dispatches about his problem traveled to the various European courts and, after much consultation, the cause of his difficulty was determined to be a tight foreskin. The King was circumcised and, judging by the Queen's subsequent letters, a complete and happy cure took place.

Of particular interest to urologists is the incidence of postprostatectomy impotence. Following simply prostatectomy, the incidence has been stated to be between 5% and 40%. However, a review of 252 patients indicated that if a man had full potency preoperatively he had only a 4% chance of becoming totally impotent following prostatectomy, irrespective of whether a transurethral resection, suprapubic prostatectomy, or retropubic prostatectomy was performed.<sup>6</sup> The physiological cause for this impotence is not apparent and, in many cases, may be due to the patient's preconceived ideas about surgery. In radical prostatectomies, however, impotence is clearly due to interruption of neural pathways, and its incidence following this surgery approaches 100%.

The association of occlusive-vascular disease and impotence has been well established since 1923 when Leriche<sup>7</sup> described his syndrome. However, the vascular causes of impotence may not always present overt clinical signs in the lower extremity or even appear as generalized occlusive-vascular disease. In these cases, specialized testing is often necessary to uncover the cause. Although there are many causes of priapism, in most cases unsuccessfully treated it will cause fibrosis within the cavernous vascular tissue and impotence. In fact, any lesion where a strong influx of blood into the corpora cavernosa is impaired may result in impotence.

Trauma is another usually obvious cause of impotence. Complete rupture of the membranous urethra causes impotence in 33% to 80% of patients due to damage to the nervi erigentes or the vessels as they pierce the perineal membrane. More recently, it has become apparent that this vascular and neurologic damage may be aggravated or even caused by the

immediate surgical repair of such trauma since these repairs result in prostatic mobilization and often further damage to the nervi erigentes.<sup>8</sup>

Patients who have systemic diseases may have a loss of libido for a variety of reasons, including metabolic and possibly hormonal mechanism disturbances. Their diminished endurance and exercise intolerance results in impotence.

Any lesion causing interruption of the nerve supply to the penis can cause impotence.<sup>9</sup> Thirty percent of patients with upper motor neuron lesions following spinal cord injury are impotent. Many paraplegics treated in our department state that although they are capable of coitus, their erections are capricious, unreliable, and unsustained. Some of the treatments used with these patients, such as bilateral pudendal neurectomies, subarachnoid blocks with alcohol, cordotomy, or sacral neurectomy, can result in impotence.

There are many drugs which may give rise to impotence (Table 1). A common one is alcohol. Alcohol can be associated with impotence in three ways: Impotence may occur: (1) during bouts of heavy drinking or (2) following alcohol-induced organ damage, or (3) the patient may use alcohol as a recourse because of psychogenic impotence.

All major endocrine abnormalities can cause impotence. It is known that testosterone is essential for potency. The majority of patients who have been castrated or who have Klinefelter's syndrome require regular doses of testosterone in order to have erections. The decreased level of serum testosterone in many impotent patients may, in reality, merely be a manifestation of the impotence and not the cause. Hence, it is not surprising that these patients do not respond to injected androgens. The most common endocrine cause of impotence is diabetes, and its incidence increases with the age of the patient: in patients between 30 and 34 years of age it is 25% while for those between 50 and 60 years it is 53% to 66%. The probable mechanism is a combination of vasculopathy and neuropathy.

### Evaluation of Impotence

The impotent patient requires a careful history and a thorough clinical examination. In addition, a psychological evaluation and specialized investigations are mandatory in determining the cause of impotence.

Preferably before seeing the physician, the patient should complete a sexual-function questionnaire (Table 2).<sup>10,11</sup> Thereafter, a full systematic history is



taken with emphasis on positive points in the questionnaire.

The patient is thoroughly examined with particular reference to the external genitalia, rectal evaluation of the prostate and seminal vesicles, the arterial pulsations in the penis and extremities, nerve sensation in the perineum, and the bulbocavernosus reflex. It is also important to examine the breasts for evidence of lactation, and the liver for enlargement.

We believe that every impotent patient should have a psychological evaluation that should be conducted by personnel experienced in sexual evaluation and counseling. In our institution, the psychological evaluation is carried out by the Division of Human Sexuality, where the patients are interviewed and undergo the following tests: Sexual Behavior Survey, the Tennessee Self Concept Scale, and Sexual Interaction Inventory, the Marital Adjustment Test,

TABLE 2

**Sexual Function Questionnaire\***

- |   |     |    |
|---|-----|----|
| 1. Describe your sexual problem and how it affects you.   |     |    |
| 2. Do you have erections under any of the following circumstances:  |     |    |
| a. Early morning?   |     |    |
| b. Masturbation?  |     |    |
| c. Anal sex?  |     |    |
| e. Female partner, other than wife?   |     |    |
| f. Male partner?  |     |    |
| g. Erotic clothing on yourself or partner?  |     |    |
| h. Vacation?  |     |    |
| i. Special places (car, hotel room, other)?   |     |    |
| j. Erotic reading?  |     |    |
| 3. Are erections good enough for vaginal intercourse?   | Yes | No |
| 4. Do you have orgasms?   | Yes | No |
| a. If so, how are they achieved?  |     |    |
| Intercourse _____   |     |    |
| Masturbation _____  |     |    |
| Oral sex _____  |     |    |
| Other _____   |     |    |
| b. Can you masturbate to orgasm but not achieve it with intercourse?  | Yes | No |
| 5. Does semen (sperm) come out of your penis?   | Yes | No |
| 6. Are you taking medicine for any of the following   |     |    |
| a. High blood pressure  | Yes | No |
| b. Sugar diabetes   | Yes | No |
| c. Nervous condition  | Yes | No |
| d. Hormone deficiency   | Yes | No |
| e. Cancer   | Yes | No |
| f. Pain   | Yes | No |
| g. Any other health problem   | Yes | No |
| 7. Have you ever had major surgery?   | Yes | No |
| 8. Have you ever had surgery on your sex organs?  | Yes | No |
| 9. Have you ever had surgery on your back?  | Yes | No |
| 10. Have you ever had a nerve disease?  | Yes | No |
| 11. How much alcohol (beer, wine, whiskey, etc.) do you consume in a week?                                      |     |    |
| 12. How strong is your desire for sexual intercourse?   |     |    |
| Slight _____  |     |    |
| Poor _____  |     |    |
| Fair _____  |     |    |
| Strong _____  |     |    |
| Very Strong _____   |     |    |
| 13. How strong is the desire of your wife or sexual partner for sexual intercourse?                             |     |    |
| Slight _____  |     |    |
| Poor _____  |     |    |
| Fair _____  |     |    |
| Strong _____  |     |    |
| Very strong _____   |     |    |
| 14. Have you consulted a psychiatrist for this problem? If so, please describe results and give name of doctor. |     |    |
| 15. Have you seen other physicians for this condition? If so, when and what therapy did you receive?            |     |    |
| 16. Would you consider an operation to provide yourself with erections?   | Yes | No |
| 17. What is your sexual partner's attitude about your having an operation to provide erections?                 |     |    |

\*Modified from Barry<sup>10</sup> and Malloy<sup>11</sup>



and the Minnesota Multiphasic Personality Inventory. Whenever possible, the psychological evaluation is conducted with both the patient and his partner. Although many of our patients have an organic basis for impotence, secondary psychological problems commonly coexist and psychological consultation becomes supportive.

All patients require urologic evaluation, not only to exclude neurogenic bladder but also to treat any coexistent obstructive uropathy because these conditions are best treated before prosthetic surgery. Urodynamic studies include cystometrograms, electromyography, bulbocavernosus reflex latency,<sup>12</sup> time-flow studies, and cystoscopy, but these are performed when indicated and not on a routine basis. At the minimum, we recommend that uroflow and residual urine studies be done.

Vasculogenic factors are evaluated with Doppler penile pressure recording in which a small blood pressure cuff is applied at the base of the penis and the arterial pressure is recorded with a Doppler flow probe. Angiography is performed when indicated. In rare cases, corporeal cavernosography is also conducted.

Karacan<sup>13</sup> has reported extensively on the use of the penile tumescence monitor. The test consists of placing a silicone mercury transducer at the base and tip of the penis. Expansion of the penis during erection is then recorded. Normally, three to five erections occur each night during the REM (rapid eye movement) phase of sleep. If there is an organic cause of impotence, erections are either diminished or absent. This test is absolutely fundamental to the investigation of impotent patients, and we perform this

test on virtually all impotent patients for two to three successive nights. Some patients with an apparently organic cause such as diabetes or multiple sclerosis have manifested normal erections when tested on the tumescence monitor. When these patients are confronted with the knowledge of their erections their functional potency often returns, either spontaneously or after psychotherapy which, after tumescence testing, they more readily accept.

### Conclusion

Impotence should be regarded as is any disease complex for which many subtle causes are possible. It requires a careful history and examination followed by a series of appropriate investigations. Since complete evaluation requires the cooperation of experienced urology and psychological testing personnel, a medical center where all necessary people and equipment are available would seem to be the most desirable type of facility at which to seek help. Treatment is dependent on the cause and consists of psychotherapy, surgical correction of local lesions, vascular surgery, or penile prosthesis when indicated. It is not within the scope of this paper to review all forms of penile prosthesis, but essentially they are of three types: paired semirigid cylinders inserted into the corpora cavernosa, paired inflatable cylinders inserted into the corpora cavernosa, or a single prosthesis inserted deep to Buck's fascia. The paired cylinders have been most efficacious with our patients so, after explaining the various benefits of each device, we allow the patient to choose between the semi-rigid and inflatable prostheses.<sup>14</sup>

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# Minnesota Medical Association

## Membership

**M**EMBERSHIP RECRUITMENT and retention has been designated a priority item by national, state, and county medical societies. Members of the Minnesota Medical Association can be proud of the leadership role their Association has taken in membership development. A suggestion in 1979 by the Minnesota Medical Association to establish a staff position to deal exclusively with membership matters led to numerous meetings with national and county societies that culminated in hiring David Luth as Director of Membership Development in March 1980. This position is jointly funded and monitored by the AMA, the MMA, and the Hennepin and Ramsey County Medical Societies.

While membership in the Minnesota Medical Association showed an increase of 162 members during 1979, there remains approximately 3200 eligible physicians in Minnesota who have not joined the county and state societies. There are approximately 4000 eligible physicians in Minnesota who are not members of the American Medical Association. These figures indicate that 25% of MMA members are not members of the AMA.

For a moment try to imagine what medicine would be like without our medical associations. There would be no unified voice to—

- speak for you at the legislature
- represent you before congress
- work effectively with HSAs
- advocate for you in an insurance crisis
- educate the public on medical issues
- represent your views to the media
- present your point of view to
  - governmental agencies
- assure quality medical education
- resist unhealthy government
  - regulation of medical practice
- update you on medical and
  - socio-economic news and issues
- answer your questions

The real question is whether you and I as individual physicians can efficiently do these things alone.

As physicians we can relate to our local county medical societies where we can more readily be a part of the policy making. This is not enough. Membership at all levels of organized medicine is essential if we, as physicians, are going to be able to project the unity of purpose and concern necessary to defend ourselves

against the attack of those attempting to fragment the profession.

Professional citizenship like political citizenship should not be fragmented. Would we be satisfied with a voice in government only at the city or county levels? Only at the state level? Or only at the national level? Most of us would feel disenfranchised if we were deprived of a voice on any of these levels. The county societies, the Minnesota Medical Association, and the American Medical Association exist because there are specific problems at each level that must be addressed in order to maintain an effective organization working for each of us.

The Minnesota Medical Association recognizes that our medical community is made up of many segments, each of which has special needs in addition to those needs recognized as common to all physicians. Such segments include VA employed physicians, HMO physicians, women physicians, physicians in training, medical students, full-time academic physicians, foreign medical graduates, and the private practitioner. The Association is aware that in the past organized medicine has not always recognized the specific needs of each of these segments, and may be at least in part responsible for the unwillingness of physicians to join. During the next few months representatives of the Minnesota Medical Association will be meeting with representatives of these sectors in an effort to identify specific needs and concerns. These needs and concerns will be studied to determine if services are presently available to meet these needs; if not, we will seek to develop appropriate guidelines and recommendations.

Organized medicine at all levels recognizes the importance of an involved active membership, and it welcomes all eligible men and women whether he or she agrees or disagrees with current policies. Indeed it is the very essence of the Associations to offer an effective democratic vehicle through which all views can be heard, debated, and acted upon.

To become a member of the Minnesota Medical Association and the American Medical Association you must first be a member of your county medical society. Membership in the Minnesota Medical Association is concurrent with your county medical society membership. This requirement is intended to foster unity of purpose and effort, and to provide you with effective representation at local, state, and national levels. To obtain more information about



## MEMBERSHIP

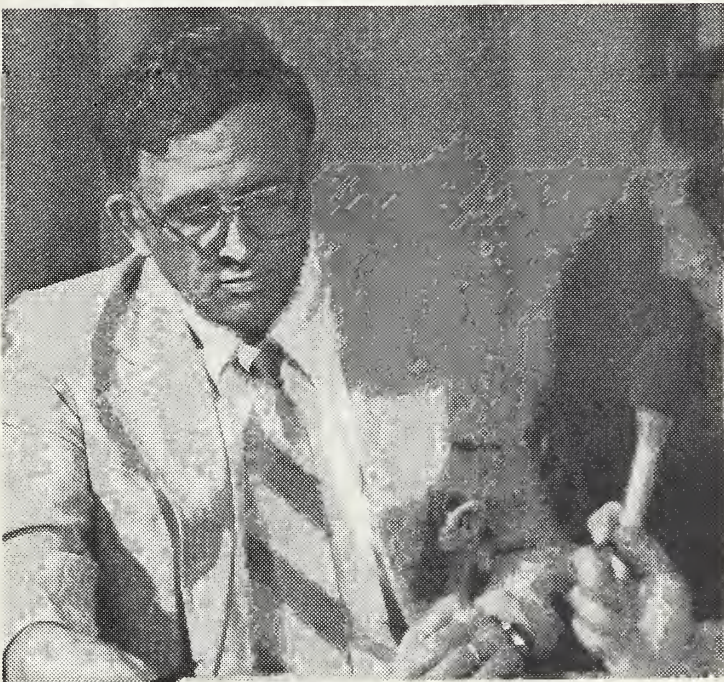
membership in organized medicine, please contact the Department of Membership Development, Minnesota Medical Association, Suite 400, 2221 University Avenue S.E., Minneapolis, Minnesota, 55414; or call: 612-378-1875.

We need organized medicine, and organized medicine needs each of us — not only our membership, but our *active participation* at the county, state, and national levels.

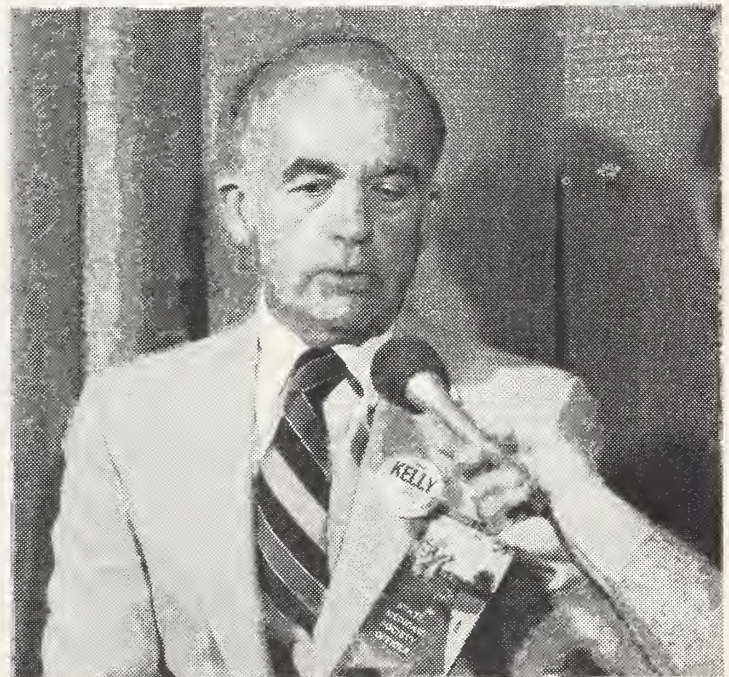
Richard P. Carroll, M.D.  
Chairman, Membership Committee,  
Minnesota Medical Association

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### Our Working MMA Officers



Dr. James F. Knapp  
Chairman, Board of Trustees



Dr. John K. Meinert  
President  
Minnesota Medical Association

At the last AMA Meeting in Chicago in July, Doctors James Knapp and John K. Meinert were interviewed by the AMA for a new series of programming called "Hometown Radio Interviews." These interviews are sent back to the hometown radio stations of the interviewed physician, in this case, Detroit Lakes and Willmar respectively.

The purpose of these interviews is to inform the physicians' home towns about important issues facing the nation currently being considered by the House of Delegates of the American Medical Association.



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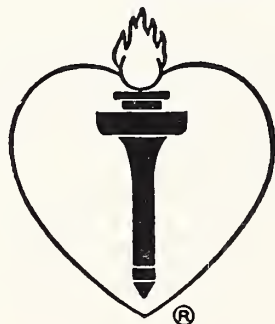
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## Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

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### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines; glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976  
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# Letters to the Editor

Dear Editors:

## In Defense of "Limbitrol"

Dr. Theodore Larson's article in the October 1979 issue of MINNESOTA MEDICINE, "Limbitrol — A Medical Dream or Nightmare," \*questioned the usefulness and safety of the combination of chlordiazepoxide and amitriptyline, suggesting instead phenothiazines and amitriptyline in combination as the treatment of choice for patients with depression associated with anxiety. In his haste to condemn this drug combination, he has overlooked the data on which the FDA based its approval of Limbitrol.

A 337-patient multicenter study showed that Limbitrol was superior to either amitriptyline or chlordiazepoxide alone in the treatment of patients with moderate to severe depression and anxiety.<sup>1</sup> In this four-way, double-blind study, parallel groups of patients were treated with either amitriptyline and chlordiazepoxide in combination, amitriptyline alone, chlordiazepoxide alone or placebo for four weeks. In no case did the dosage exceed six (6) tablets of Limbitrol 10-25 daily, (the average dosage was 4.4 tablets daily). Many physicians who have been using Limbitrol in their practices confirm the study results in that their patients require no more than six (6) Limbitrol 10-25 daily, and the average daily dosage appears to be even less than the 4.4 tablets daily reported in the multicenter study.

Several of Dr. Larson's concerns "potential hazards" were based on the assumption that the daily dose of chlordiazepoxide taken with Limbitrol would be far in excess of 60 mg. Not only would those large doses be outside of the dosage level suggested in the Limbitrol package insert, but as noted above, they are outside of the dosage level found to be effective in the clinical testing of the drug.

Although withdrawal symptoms from Limbitrol have not been reported, withdrawal symptoms following abrupt cessation of either component alone have been reported. Physical and psychological dependence have rarely been reported in persons taking recommended doses of chlordiazepoxide, so caution must be exercised in administering Limbitrol to individual's known to be addiction-prone or to those whose history suggests they may increase the dosage on their own.

As with any psychoactive medication, it is suggested that when using Limbitrol after the symptoms are controlled, the dosage should be decreased to the smallest amount required to maintain symptom remission. And again, as with all psychoactive medications, it is suggested that change in the dose and/or discontinuation of the medication should be gradual.

Another important advantage of Limbitrol over amitriptyline, as demonstrated in the multicenter study, is that the therapeutic response to Limbitrol occurs earlier and with fewer treatment failures.

It is interesting to note that although Dr. Larson suggested the use of phenothiazines for the treatment of these patients, in an article about "Hazards," he failed to mention the substantial risk of extra-pyramidal side effects, especially tardive dyskinesia, that are well known to be associated with the use of this class of drugs.

Richard G. Dudley, Jr., M.D.  
Assistant Director  
Professional Services  
Roche Laboratories

\*See page 725.

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# LETTERS TO THE EDITOR

Dear Editors:

In response to Richard G. Dudley, Jr., M.D. of Roche Laboratories and his defense of Limbitrol, Dr. Dudley does not address the main concern in my paper, i.e. the long-term use of Limbitrol.

Studies so far seem to be limited to four week trials. Four weeks is an inadequate course of treatment for most cases of moderate to severe depression which require tricyclic antidepressant therapy.

Long-term Limbitrol treatment of depression apparently has not been studied or at least not reported. The potential hazards of Limbitrol therapy mentioned in my paper will exist until data proves that such hazards do not exist.

No drug is completely safe. Phenothiazines do have the potential of producing serious side effects. The clinician and the patient must be alert to these complications. However, phenothiazines are not addictive. With proper care and observation of the patient they are relatively safe to use in long-term therapy.

Theodore G. Larson, M.D.  
St. Cloud, Minnesota

Dear Editors:

## Rural Physician Associate Program

The Rural Physician Associate Program (RPAP) is where some of the flowers grow. Here are some of the figures showing almost 70% of our students are back in rural Minnesota and the U.S.A. Keep up the good work! These are results up to 7-1-80.

Jack Verby, M.D.  
Professor, Department of Family Practice and Community Health  
University of Minnesota

### Rural Physician Associate Program Outcomes

1971-80

(N = 318)

RPAP Students During the 1979-80 Academic Year (N = 40)

Current Status of Former RPAP Students (N = 278)

<u>Class of</u>	<u>In Practice</u>	<u>In Residency</u>	<u>Med School</u>	<u>Other</u>
1971-72	22	0	0	1
1972-73	34	3	0	0
1973-74	20	6	0	0
1974-75	27	9	0	1
1975-76	2	38	0	0
1976-77	0	40	0	0
1977-78	0	37	1	0
1978-79	0	1	36	0
	<u>105</u>	<u>134</u>	<u>37</u>	<u>2</u>

In Practice:

	<u>Number</u>	<u>Percent</u>
Minnesota Rural Locations	51	50%
Out-of-State Rural Locations	16	16%
Minnesota Metro Locations	24	22%
Out-of-State Metro Locations	14	12%

In Residency Training

Family Practice	76	Radiology	2
Medicine	28	Pediatrics	2
Surgery	10	Neurology	2
Flexible	4	Anesthesiology	2
Ob-Gynecology	3	Orthopedics	1
Psychiatry	3	Hematology	1

In Medical School

Phase D<sub>4</sub> = 37 students

Other:

1 Dropped out of medical school  
1 Deceased



# Medical Grand Rounds

## Infection with "Atypical" Mycobacteria

CHARLES DRAGE, M.D.\* and FRANK MACDONALD, M.D.†

Editor: Robert J. McCollister, M.D.

"Atypical" mycobacteria are now found in approximately half of the positive cultures obtained from patients suspected of having tuberculosis at the University of Minnesota Hospitals. Some "atypical" organisms are pathogens and some are only saprophytes and/or contaminants. The decision as to whether an "atypical" organism is a pathogen or a saprophyte is often difficult. The treatment of "atypical" mycobacterial infections is challenging and often requires use of several drugs in combination as well as surgery. Because the management is complex and changing, these patients should be treated by a physician with experience with these diseases. This grand rounds includes a discussion of the classification of these organisms and reports of several patients with difficult problems in clinical diagnosis and management.

**Dr. Charles Drage:** The "atypical" mycobacteria are acid-fast organisms which resemble tubercle bacilli in some respects but are atypical in others. They have also been called anonymous, opportunistic, and unclassified, but these terms are misleading and not helpful in identifying or classifying the organisms. Improved laboratory methods have resulted in detection of increasing numbers of patients with atypical mycobacterial infections at the University and the Veterans Administration Hospitals. After Dr. Richard Kronenberg presents the first patient, we shall review the etiology, classification, and diagnosis of atypical mycobacterial infections and discuss treatment of three additional patients with illustrative problems.

### Case-Report

#### *Patient 1*

**Dr. Kronenberg:** A 43-year-old truck driver, who had been in apparent good health, developed fever and left lower lobe pneumonia in March, 1977. The chest x-ray (Figure 1) showed bilateral diffuse fibronodular infiltrates and consolidation in the left lower lung field. The patient recalled a history of a seemingly minor problem with dysphagia and this then led to the diagnosis of achalasia. Sputum cultures grew *Mycobacterium fortuitum*. In April, a myotomy of the lower esophagus and a biopsy of the left lower lobe were done. On sectioning, the lung showed aspiration pneumonia and necrotic granulomas. After the patient was transferred to University Hospitals, there were

many futile attempts with many antibiotics, to control his persistent daily fever spikes, which reached levels of 104°F. We thought that a pus pocket in his left pleural space most likely was causing the fever. Finally, after several unsuccessful chest taps under fluoroscopic control, pus was obtained and the patient was transferred to the surgical service for open drainage. The patient gradually improved, gained weight, and felt much better. He was discharged from

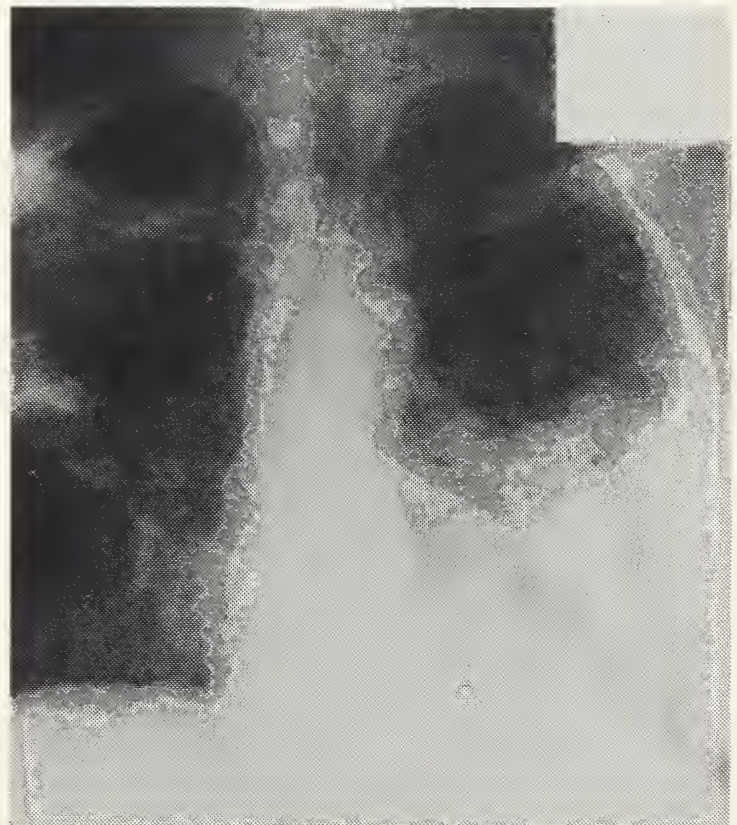


Fig. 1—Laparoscopic instruments. Sheathed trochar (upper); laparoscope (lower).

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the hospital on antibiotic therapy. Persistent daily fevers to 100 to 101 degrees F. were thought to be related to the unresolved pulmonary infiltrate. During this patient's illness, *M. fortuitum* was grown from eight sputum cultures, from a food particle that was coughed up, three pleural fluid specimens, a pleural biopsy culture, two wound cultures, and two lung biopsies. Sensitivity testing done at the Veterans Administration Hospital laboratory showed the organisms to be resistant to every known antituberculous drug.

**Dr. Drage:** You can see what a difficult management problem this kind of patient presents. This organism, *M. fortuitum*, is ubiquitous and is usually considered a saprophyte, but here it was clearly pathogenic. These patients can be extremely difficult to treat because these organisms may be partially or completely resistant to antituberculous chemotherapy. There is one report in the literature of a patient with pulmonary infection with *M. fortuitum* associated with achalasia plus another patient treated at the Veterans Administration Hospital for an infection with *M. fortuitum* in association with achalasia and this patient make a total of three reports of this curious association. If this is a predisposition, it has not been recognized heretofore.

The atypical mycobacterial organisms from human sources were first recognized in the mid-1930s by Pinner. These mycobacteria were not pathogenic for guinea pigs and were thought to be saprophytes, fellow travelers with *Mycobacterium tuberculosis*. Not until the early 1950s was it recognized that some patients who appeared to have typical pulmonary tuberculosis actually had disease caused by organisms with different cultural, pigment and biochemical characteristics, the “atypical” mycobacteria. The standard classification of these bacteria, devised by Runyon, (Table 1) is in current use, but is changing rapidly and will likely be completely revised.

At the University Hospitals between 1975 and 1977, mycobacteria have been isolated from cultures from 32

patients, and in 15 of these patients, nearly half the total, the organism was one of the “atypical” varieties, commonly one of the *M. battey-avium* complex.

### Group I Photochromogens

These organisms produce pigment when exposed to light. In Minnesota, approximately half of the cases of “atypical” pulmonary tuberculosis are caused by *M. kansasii*. Clinically, these patients greatly resemble patients with *M. tuberculosis*. Therefore, when *M. kansasii* is isolated from such a patient who is suspected of having pulmonary tuberculosis, it should be considered a potential pathogen. *M. kansasii* has been isolated from tap water, and from cows and pigs but not from soil. It is found in the Midwest and in Texas where it is very common. In some studies in larger communities, from 80 to 90% of the people tested have a positive skin test to the antigen from this organism. On acid-fast smears, which, incidentally the physician should examine, the organisms are characteristically banded and quite large.

*M. marinum* causes nodular lesions on the fingers, knees, and elbows, and can be isolated from these lesions. It has been found in ponds, swimming pools, and fishtanks. There have been numerous reports of *M. marinum* infections traced to home aquaria. One swimming pool was implicated as a common source in an outbreak of over 100 cases. Some of these skin lesions spontaneously remit, some respond to the newer drugs, and others require both drugs and surgery.

*M. ulcerans* is an interesting organism, seen in many areas of the world. This organism is endemic in the upper Nile where it is a common cause of infections, causing burrowing ulcers which may extend through the skin and subcutaneous tissue down to the muscle fascia.

### Group II Scotochromogens

These organisms produce yellow or orange pigment without being exposed to light. The potential pathogen in this group is *M. scrofulaceum*, which can cause cervical adenitis, particularly in children. Pulmonary involvement and skin abscesses are quite rare. It is isolated from water, food, and soil, and it may be found in sputum from patients with no evident pulmonary disease. One patient at the University Hospitals was thought to have sarcoidosis at mediastinoscopy, but *M. scrofulaceum* was grown from a node biopsy culture. This organism is quite resistant to the usual drugs. Often, resection of the infected nodes is necessary for cure.

TABLE 1

#### “Atypical” Mycobacteria

Group I	Photochromogenic pigment on exposure to light	<i>M. kansasii</i> <i>M. marinum</i> <i>M. ulcerans</i>
Group II	Scotochromogenic yellow, orange, brick red pigment	<i>M. scrofulaceum</i>
Group III	Nonchromogenic	<i>M. intracellulare</i> ( <i>M. battey-M. avium</i> complex) <i>M. xenopi</i>
Group IV	Rapid growers	<i>M. fortuitum</i>



### Group III Non-chromogens

In Minnesota, about half the atypical mycobacteria isolated are *M. intracellulare*, reported by the State Board of Health as the Battey-avium complex. Many laboratory characteristics of these two organisms are the same, but they can be distinguished serologically. Pulmonary infection, again indistinguishable from that caused by *M. tuberculosis*, is the most common form of disease. In the southeast U.S., 65% of the young men who have been tested are skin positive to PPD-B, an antigen made from the protein from *M. intracellulare*.

*M. xenopi* has not been seen yet in Minnesota though we recently suspected it as the agent in one case in the Twin Cities. Increasingly, it is being reported from southern England and Europe, where it has been isolated from rivers and the coastal areas. It seems to be an organism that is found in water.

### Group IV Rapid Growers

There are at least three organisms which are not now differentiated from *M. fortuitum* on culture. These organisms are truly ubiquitous and are frequently reported in cultures where they are almost always, but not always, saprophytes. Although rarely a cause of disease in humans, *M. fortuitum* can cause lung, skin, or eye lesions. The first case presented today was caused by this organism.

Physicians in Minnesota must consider, for practical purposes, the seven mycobacterial pathogens listed in Table 2 as the species responsible for “atypical” mycobacterial disease in this area.

Species which have been reported to cause disease in humans which have yet to be reported in Minnesota include *M. xenopi* and *M. simiae*, a newly identified organism that has been isolated from monkeys and has caused disease in man. *M. szulgai* is another newly recognized organism that has been identified as potentially pathogenic in man.<sup>1</sup> No known cases have been seen in Minnesota.

Besides the potential pathogens, there is a large number of mycobacteria which can be cultured and are totally saprophytic, such as *M. smegmaceae*, *M. gordonae*, found in tapwater, and *M. triviale*.

The following points should be kept in mind regarding “atypical” mycobacteria:

1. “Atypical” mycobacteria are not thought to cause disease transmitted from person to person.
2. Many persons harbor the organisms without having any evident disease. In a study done in 1960 in the Robbinsdale school district, skin

tests of 15-year-olds showed less than 2% positive response to *M. tuberculosis*, 2% positive to photochromogens (*M. kansasii*), 20% positive to scotochromogens and 16% to *M. intracellulare* (Battey-avium). You can see from these epidemiological studies of a young age group that many people are being exposed to and subclinically infected by these organisms.

3. Pulmonary infection is often associated with pre-existing lung disease, such as silicosis, coal-workers’ pneumoconiosis, chronic obstructive lung disease and for that matter, either treated or untreated *M. tuberculosis*.

TABLE 2

Seven Mycobacterial Species Which Have Caused Disease in Minnesota:

*M. tuberculosis*  
*M. bovis*  
*M. kansasii*  
*M. intracellulare* (Battey-avium complex)  
*M. fortuitum* (lung)  
*M. scrofulaceum* (lymph node)  
*M. marinum* (skin)

Species Which Have Been Reported to Cause Human Infection Elsewhere in the World:

*M. ulcerans* (skin)  
*M. xenopi* (lung)  
*M. szulgai* (lung)  
*M. simiae* (lung)

4. There is a large marked cross sensitivity between the antigens of *M. tuberculosis* and the “atypical” mycobacteria, and the sensitization to the infecting agent is usually greater. Incidentally, this has been very helpful in epidemiological work. For instance, if a patient has been infected by *M. battey*, the skin test to this antigen usually will be larger than to *M. tuberculosis* even though there is cross sensitivity.
5. “Atypical” mycobacteria pathogenic for man may be ubiquitous and are true saprophytes in certain environments. It may be very difficult to prove a causal relationship between these organisms and disease.
6. Atypical<sup>2</sup> organisms usually show marked or complete resistance to chemotherapy.

**Dr. Frank MacDonald:** At the Veterans Administration Hospital, we’ve been fortunate to have had a specialized laboratory for the study and identification of mycobacteria which has been developed by Drs. Wendell Hall and Horace Zinneman and Mr. Oscar Jones. The Runyon classification is related to pigment production, but this is being greatly changed by newer methods of numerical taxonomy, and it is now quite



clear that different members of a given cluster may or may not produce pigment. Thus, pigment production is not a completely reliable characteristic. The newer classifications<sup>2</sup> may help us to predict better whether an organism is likely to infect humans and so they may be more helpful clinically. Some important laboratory characteristics of the mycobacteria are outlined in Table 3.

In our experience at the Veterans Administration Hospital, there have been 32 patients with atypical mycobacterial infections, 15 with *M. intracellulare* infection, 14 with *M. kansasii*, the *M. fortuitum* that was mentioned, and two that don't fit nicely into known species. *M. intracellulare* represents our biggest problem in therapy, with reports of success with multiple drugs ranging from 30 to 73%. These results are rather poor, and this is reflected in our experience. We have successfully treated eight of 14 patients with drugs. The Denver group has had the best results, using combinations of from four to six drugs, combining these to which the organisms appear susceptible with others to which organisms appear resistant, usually including isoniazid (INH), streptomycin, and ethambutol. Such drugs may have a greater effect in combination than might be expected from the sum of individual sensitivities. The reason for this is unknown although multiple sublethal points of damage to the metabolism of bacteria may add up to a critical effect. Other drugs now being studied but not yet developed for use in mycobacterial infections include erythromycin, which has been shown to be effective with many strains *in vitro*. We found four of six cultures sensitive to moderate levels of the drug. We have added it to the therapy of three patients but cannot yet say whether it is of any help. Capreomycin

and kanamycin have occasionally been reported to show some effect. Certain antileprosy drugs of the riminophenazine group have had a very limited clinical trial. In the remaining six of our patients, all chemotherapy failures, surgery was more or less successful in four. Two of our patients have persisting chronically active disease. Chemotherapy coverage of the post-surgical period is important but it is often difficult. When post-surgical relapses occur it is usually because of inadequate chemotherapy coverage. We feel that surgery may be indicated in patients who are chemotherapy failures. As to indications for surgical resection, we're really not sure from our experience that positive sputum cultures are a good indication for surgery in a patient who is doing well clinically.

In contrast to *M. intracellulare*, *M. kansasii* infection is quite a different story. Even though this organism is not quite as responsive to therapy as is *M. tuberculosis*, our results have been surprisingly good. In 11 out of 12 patients, drugs were successful in conversion of the sputum and control of the disease. These results are fairly typical; other groups report 90% success or greater, if ethionamide or rifampin are members of the therapeutic regimen. To treat *M. kansasii* infections, we have used three drugs — INH, rifampin, and ethionamide together. These agents usually look best in laboratory testing, and their use in combination seems to contribute to the very good results. Ethambutol and streptomycin may be of use in selected cases. In one patient, surgery for diagnosis was followed by chemotherapy. As to the past medical history, two of our patients have silicosis, six worked in dusty occupations without developing silicosis, three have had a gastrectomy, 10 were alcoholic, five had chronic obstructive lung disease. Thus, it seems

TABLE 3  
Laboratory Differentiation of Mycobacteria (Acid-Fast Bacilli)

Acid fast morphology	<i>M. tuberculosis</i> corded	"Atypical" Mycobacteria banded ( <i>M. kansasii</i> ) curved ( <i>M. xenopi</i> )
Colonies	rough	mainly smooth
Pigment	buff	yellow-orange in dark ( <i>M. scrofulaceum</i> ) yellow in light ( <i>M. kansasii</i> ) buff ( <i>M. intracellulare</i> )
Niacin production	positive	negative (except <i>M. simiae</i> )
Growth rate	slow	slow in most fast ( <i>M. fortuitum</i> )
Temperature optimum	37°C.	25°C. (except <i>M. avium</i> best at > 37°C.)
Iron uptake	—	positive ( <i>M. fortuitum</i> )
Susceptibility to anti-tuberculosis drugs	susceptible	resistant to most ( <i>M. kansasii</i> susceptible to rifampin, ethionamide)



that many of our patients may have had impaired resistance and that the term opportunist might well be applied to *M. kansasii*.

#### Patient 2

**Dr. Tom McGowan:** A 30-year-old white repair man was referred from the Sioux Falls Veterans Administration Hospital for evaluation of possible tuberculosis because of fibronodular infiltrate in the right upper lobe noted on a routine chest Xray in November of 1969 and again in February of 1970. The patient was seen at the Minneapolis Veterans Administration Hospital in September 1970. He had noted only mild fatigue and intermittent non-productive cough, was on no medication at that time, and had no allergies. He had heard that his grandfather might have died of tuberculosis. There was a 15 pack year smoking history. The past medical history and review of systems were noncontributory. His physical examination was within normal limits. Chest Xray (Figure 2) revealed an infiltrate in the right upper lobe. Of multiple sputa for bacterial, fungal, and acid-fast (AFB) studies, only one out of the initial five AFB smears was positive. Intermediate strength PPD tests were 7 and 5 mm. respectively. Fungal serology studies were negative. Treatment was begun with INH,



Fig. 2—Laparoscope in abdomen, with pneumoperitoneum. Range of vision shown between dashed lines

300 mgm daily and ethambutol, 1000 mgm daily. Later, five of the sputum cultures were reported positive for *M. kansasii*, sensitive to ethionamide, partially sensitive to rifampin and cycloserine and resistant to streptomycin, INH, PAS, ethambutol, and capriomycin. Treatment was then altered. Ethambutol was stopped, the INH was continued and ethionamide 250 mgm t.i.d. and cycloserine 250 mgm b.i.d. were started. Cultures became negative after six months, but the treatment was continued for an additional year. Later, the chest Xray showed only residual fibrosis.

**Dr. MacDonald:** This is a fairly typical case of *M. kansasii* infection although he is a bit younger than most of our patients, whose mean age was 53. But this radiologic pattern is quite familiar. Most patients at our hospital had minimal to moderately advanced disease. The culture sensitivities were characteristic of this organism. He did not receive rifampin, which was not then available. Ethionamide was given, to which his organism was fully susceptible. What should have been done if this patient were seen now and had failed to respond to initial chemotherapy? Should we have added rifampin, which is an excellent drug in this infection? In the treatment of *M. tuberculosis* infection, the addition of a single drug to a failing regimen often leads to rapid emergence of resistance to the new drug and to therapeutic failure. Davidson in Denver has reported a similar experience in the treatment of *M. kansasii* infection. In two patients, rifampin resistance emerged during single drug treatment with rifampin. From this we must assume that we should never add a single drug, even rifampin, to a failing regimen in a *M. kansasii* infection.<sup>3</sup>

#### Patient 3

**Dr. Gregory Beall:** This 60-year-old man had worked for over 30 years as an arc welder. He was admitted to the Veterans Administration Hospital in October, 1976 with a one-month history of blood streaked sputum. There was a past history of a chronic cough productive of a small amount of whitish sputum, but the hemoptysis was new. There had been no fever, chills, weight loss, or chest pain and no history of TB exposure. Pertinent past history included a history of depression which required treatment with electroshock therapy in 1970. He smoked a pipe and inhaled, and had been an arc welder for some 35 years in a dusty shop, but there was no exposure to silica. Physical exam on admission in October was unremarkable except for a few scattered rhonchi throughout the lungs. FEV-1 was 1.8 liters, FEV-T, 2.4 liters. The skin test with intermediate PPD was negative, mumps



and candida were positive. Five of six AFB smears were positive. The Xray showed a nodular infiltrate in the right upper lobe and probably in the left upper lobe (Figure 3). In addition there was a diffuse increase in interstitial markings interpreted as interstitial fibrosis. INH, ethambutol, and rifampin were started and by January, 1977 all AFB cultures were negative and the hemoptysis disappeared. In early February, 1977, he was admitted to St. Paul-Ramsey Hospital with an acute depression. Since this may have been due to the INH, the drug was stopped. The cultures remained negative, but because of the Xrays, which did not change, erythromycin and streptomycin were added in April. In the most recent film, in July 1977, there is no significant change and the infiltrate persists. To date, these microorganisms have not been classified. The Veterans Administration reference laboratory in California stated that they resembled *M. simiae*, but biochemical studies here were more suggestive of the *M. intracellulare* group. Sensitivities to multiple drugs showed general resistance, except for streptomycin.

**Dr. MacDonald:** The problem identifying this patient's organism has been the disagreement on whether it is a significant niacin producer or not. Most niacin positive mycobacteria are *M. tuberculosis*, but the newly recognized species *M. simiae* is also

strongly positive. In this case *M. simiae* is not a good possibility, because none of the other biochemical tests are in agreement with the usual findings with this organism. Perhaps it is a variant of *M. intracellulare*, but we don't know.

His interstitial process and welding exposure suggest that he has welder's lung, which is probably due to deposition of iron. This is a rather non-reactive material and does not produce much disability. Chest Xrays look worse than results of pulmonary function studies. Some reports show a relationship between opportunistic mycobacterial infections and silicosis. Marx and others in England have recently found that work in a dusty trade such as sandblasting, foundry work, ceramic work, even without the appearance of clinical pneumoconiosis is associated with increased risk of opportunistic mycobacterial infection. It is not known whether this is related to the overwhelming of macrophage defenses.

Whether we will succeed therapeutically in this patient is still in question. Drug toxicities are a frequent problem in this type of infection, and may limit the drugs which can be used, as was the case with this patient. His depressive reaction was probably related to INH, and several other antimycobacterial agents can produce similar side effects. The prognosis in this patient must be guarded.

#### *Patient 4*

**Dr. John Stevenson:** This 34-year-old man had juvenile onset diabetes mellitus which was very difficult to control, perhaps related in part to his mild retardation. When first seen at the University Hospitals in 1971, there was an infiltrate in his right upper lobe. Because skin tests for TB were negative, no sputum cultures were done. In 1973, he returned with pulmonary complaints and a history of gradual weight loss and weakness for at least six months. The chest Xray revealed progression of the right upper lobe infiltrate (Figure 4). Intermediate and second strength skin tests for TB were again negative but several sputum smears were positive for AFB. He was discharged on fairly standard treatment for tuberculosis: INH, ethambutol, and rifampin. The patient was readmitted after the sputum cultures were reported to be growing Runyon group III non-chromogens of the Battey-avian complex, (*M. intracellulare*). The patient's status was unchanged, although he had had continued difficulty with his diabetes, with frequent reactions and episodes of ketoacidosis as well. Since there had been reports of success with a five drug regimen, which included rifampin, INH, and etham-



Fig. 3—Laparoscopic view of normal structures: liver (left), lesser curve of stomach (right, lower), diaphragm (above), spleen tip (right).



butol plus streptomycin and pyrazinamide, the latter two drugs were added. Because of his poorly controlled diabetes and his mental retardation, there was real question as to how reliably he could be expected to stick to a very difficult drug regimen. Because the disease was fairly well localized, it was elected to combine surgical treatment early in the course of his illness with a five drug treatment program. At the time, about the best results that could be achieved in terms of sputum conversion, even with the very aggressive five drug treatment program, were in the range of 75%. Because of his diabetes and his unreliability, it was elected to do a lobectomy. Following surgery, he had a massive pulmonary embolus which required emergency embolectomy. He had, as well, episodes of atelectasis and pneumonia. After discharge, he did very well. His personal physician, using meticulous care, supervised an outpatient drug treatment program. Pyrazinamide has a 10% incidence of severe liver toxicity, and some recommend that it should not be given outside the hospital. If the drug is not stopped at the first signs of toxicity, many patients do poorly and some die. This patient was maintained on the drug for several years with close followup by his personal physician. Streptomycin was stopped because of a reaction to it, and after three years, all his antimycobacterial medications were stopped. He has continued to do

well, and his diabetes has been in better control. This patient with atypical mycobacterial disease caused by a species which is particularly difficult to treat with chemotherapy was managed successfully with a very aggressive combination drug and surgery treatment program.

**Dr. Drage:** This disease was progressing even when he was on five drugs. It was very difficult for this man to take this medication, and at one time he would have had to have been in the hospital. This case points out that surgical intervention can stop the progress of this disease. But it also is not without hazard. Complications are unusual, but chest surgery has a morbidity and potential mortality which cannot be taken lightly.

**Dr. MacDonald:** I cannot say that this patient might have responded to conservative chemotherapy, if you can call five or six drugs conservative. As to the surgical complications I have seen, the specific infectious complications are greater in these patients than in those with *M. tuberculosis* infection. We have also seen failure of surgery to convert sputum, and early relapse. This is because we don't have adequate chemotherapy to cover the possibility of surgical breakdown. It is almost as it was with tuberculosis before chemotherapy was adequate, where we had surgical failures due to poor chemotherapy coverage. Surgery in mycobacterioses has to be undertaken with the knowledge that it is not going to be the whole answer and that there is likely a greater incidence of complications.

**Question:** What was the course of this group of diseases before chemotherapy was used?

**Dr. MacDonald:** The disease wasn't recognized before we had TB therapy. The bacteriologist used to be told to throw these cultures out before physicians heard about them. In the days when we used only INH and PAS, the results were poorer. The National Jewish Hospital really is the one place where enough of this is seen to tell us something about it, and their results of 75% or so of chemotherapy conversions are a lot better than the results that we and others have using less ambitious chemotherapy programs. Theirs is not a controlled series, in fact there are no controlled series,<sup>4</sup> so there is no answer other than an impression. Apparently something they do really works, and probably it is the five drugs in combination, but it is a question that one could legitimately be very skeptical about. Interestingly, many of these drugs often completely fail to inhibit the organism in the test tube, even at higher concentrations than can be achieved in vivo. There are some studies in animals showing that



Fig. 4—Laparoscopic view of nodular liver.



combinations of drugs to which organisms are resistant in vitro give better results in treatment.

**Question:** Are atypical antigens useful in skin testing?

**Dr. Drage:** I think for epidemiological purposes, it has proved very helpful, at least in plotting endemic areas of infectivity of these organisms. And it has also helped us to interpret the tests in patients who show a doubtful reaction to intermediate strength PPD and a

positive one to second strength PPD. This combination usually means prior infection with a “atypical” organism. In fact, I think skin testing with second strength PPD probably should not be done in most cases. It’s not particularly helpful, and we’ve had several severe reactions with local and systemic symptoms. The best procedure to use to follow up a doubtful intermediate PPD is to apply skin tests using “atypical” antigens.

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# Pathologic Anatomy

## Primary Mediastinal Embryonal Carcinoma

MARK R. WICK, M.D.\* and GENE P. SIEGAL, M.D., PH.D.†

Embryonal carcinomas may arise in the mediastinum, in the absence of concomitant gonadal neoplasms. These mediastinal lesions have a prognosis which is worse than that of identical growths in the testis or ovary. Males are predominantly affected, usually in the third or fourth decade of life. The tumors are not uncommonly asymptomatic, and they are usually of considerable size upon initial diagnosis. Tumor secretory products may be associated with such neoplasms, and these products are often capable of effecting physiologic changes in the host. Treatment at present is usually palliative, and most individuals with mediastinal embryonal carcinomas die within two years after diagnosis. A case report is presented of a 19-year-old man with such a lesion, which resulted in his death 22 months after discovery of the tumor.

ALL STUDENTS OF thoracic diseases are familiar with the three "Ts" of the anterior mediastinum: retrosternal thyroid, thymic masses, and teratomas. The presence within the thorax of the last member in this diagnostic triad is related to the embryologic origin of teratomas in the midlines germinal ridges.<sup>1,2</sup> Remnants of these ridges may later give rise to primary mediastinal, retroperitoneal, and pineal germ cell tumors, as well as gonadal neoplasms of the same type.

Of all mediastinal teratomas, 90% are cystic and benign.<sup>3</sup> Among the malignant germ cell counterparts of such growths, seminomas, embryonal carcinomas, and choriocarcinomas may all be found as primary tumors in the mediastinum.<sup>4,5</sup> Commonly, two of these histologic types are mixed within the same lesion. The age and sex statistics of patients with these tumors mimic those associated with primary gonadal tumors of identical histology.<sup>6-8</sup> Males predominate usually in the third or fourth decade of life. The relative frequency in the mediastinum of the histopathologic variants given above also parallels that of identical neoplasms in the testes or ovaries; seminomas are most common, and choriocarcinomas are least common. The case to be presented deals with the statistical intermediary of this group, a primary embryonal carcinoma of the anterior mediastinum.

### Case Report

A 19-year-old white male felt well when a chest roentgenogram taken during an Armed Forces induction examination revealed a large anterior mediastinal mass. He was referred to our institution in July 1975.

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The patient related that for several weeks, he had noted mild periorbital and facial edema upon arising in the morning. In addition, he had become slightly dyspneic upon running one-half mile, representing a change from his usual exercise tolerance. The past medical history and review of systems were otherwise unremarkable.



Fig. 1 — Gross appearance of thoracic viscera at autopsy. Note the large anterior mediastinal tumor mass (T) adherent to and invading the heart. The lungs (L) are markedly consolidated.



Physical examination showed a muscular, healthy-looking young man with normal vital signs. The neck veins were mildly distended in both the supine and erect positions. There was no lymphadenopathy, and the testes were of normal size and consistency, without masses. The remainder of the physical examination was normal as well.

Laboratory test results were all within normal limits. A repeat chest roentgenogram confirmed the presence of a superior and anterior mediastinal mass, with bilateral lymphadenopathy.

Diagnostic mediastinoscopy was performed. A huge mediastinal mass was encountered obstructing the superior vena cava. A biopsy of the tumor was interpreted as "anaplastic seminoma," apparently primary in the mediastinum. Because of the histology and infiltrative nature of the lesion, the surgeon felt that a thoracotomy and resection of the mass were not indicated.

Postoperatively, the patient had an acute exacerbation of his superior vena caval syndrome, with cyanosis and upper airway edema. Radiotherapy to the mediastinum was initiated on an emergent basis, with some relief of this problem. A bone survey series of roentgenograms and a lymphangiogram were interpreted as normal.

Over a three-month period, 5700 R were delivered to the mediastinum (1400 R for four doses, separated by two week rest periods). There was essentially no change in the size of the mass radiographically during this time.

In February 1976, acute dyspnea appeared. Physical examination revealed Kussmaul's sign, and a pericardial friction rub was audible. An echocardiogram showed a large pericardial effusion. A thoracotomy was performed, and pericardial drainage windows were created. There was no neoplastic involvement of the pericardium, and the mediastinal mass was unchanged from its original size. Postoperatively, combination chemotherapy with bleomycin, adriamycin, and cisdiaminodichloroplatinum was initiated.

The patient refused further chemotherapy in March 1977. Bilateral reticular infiltrates seen in the lungs at this time radiographically were felt to represent a combination of radiotherapy and chemotherapy-induced interstitial fibrosis. A confirmatory lung biopsy was not performed.

The patient's symptomatic and functional status was stable until April 1977, when severe dyspnea abruptly appeared, without amelioration by oxygen given with nasal cannulae at his home. Physical examination upon subsequent hospitalization on May 1, 1977 revealed a blood pressure of 90/40, pulse of 125/min, and respiratory rate of 56/min. He was afebrile. Marked cyanosis,

jugular venous distention, and absent breath sounds over the left hemithorax were observed. A protodiastolic gallop sound was audible upon cardiac examination.

A chest roentgenogram showed bilateral large pleural effusions. Laboratory test results included a hemoglobin of 12.7 g, white blood cell count of 17,000/mm<sup>3</sup> with a left shift, platelet count of 70,000/mm<sup>3</sup>, activated partial thromboplastin time of 109 sec, and plasma bicarbonate of 14 meq/l. The anion gap was 23. An echocardiogram did not suggest recurrent pericardial effusion. Fibrin split products and fibrinogen were not measured, but a hypocoagulable state was observed clinically.

A diagnosis of acute bronchopneumonia, superimposed upon chronic pulmonary insufficiency, was made. One day after admission, a left thoracentesis, done in an effort to partially relieve the patient's dyspnea, resulted in a pneumothorax. After administration of fresh frozen plasma, a chest tube was inserted. Shortly afterward, the patient became severely cyanotic and suffered a fatal cardiopulmonary arrest.

A complete autopsy revealed an extensive, largely necrotic tumor mass in the mediastinum, invading the myocardium (Figure 1). Extrathoracic metastases were not found, the testes were free of masses, and gynecomastia was not present. The pituitary and pineal glands were unremarkable. The lungs showed severe interstitial fibrosis and acute confluent bronchopneumonia. Fibrous pleuritis and pericarditis were evident. The remainder of the postmortem examination did not disclose any other abnormalities.

Histopathologically, the mediastinal tumor was composed of large polyhedral cells with eosinophilic cytoplasm, prominent nucleoli, and numerous mitoses. The cells were arranged in sheets, cords, and primitive gland and ductlike structures (Figures 2-3). They stained positively with the periodic acid-Schiff reaction. Review of the biopsy specimen obtained at mediastinoscopy disclosed small areas in the tumor with a similar appearance to the tissue described above. Multiple microscopic sections of both testes were completely normal. Based on the histologic features of the neoplasm and its clinical behavior, it was thought that embryonal carcinoma represented the best final diagnosis for the primary mediastinal neoplasm.

## Discussion

Though germ cell tumors of the mediastinum are identical to those of the gonads in histologic and

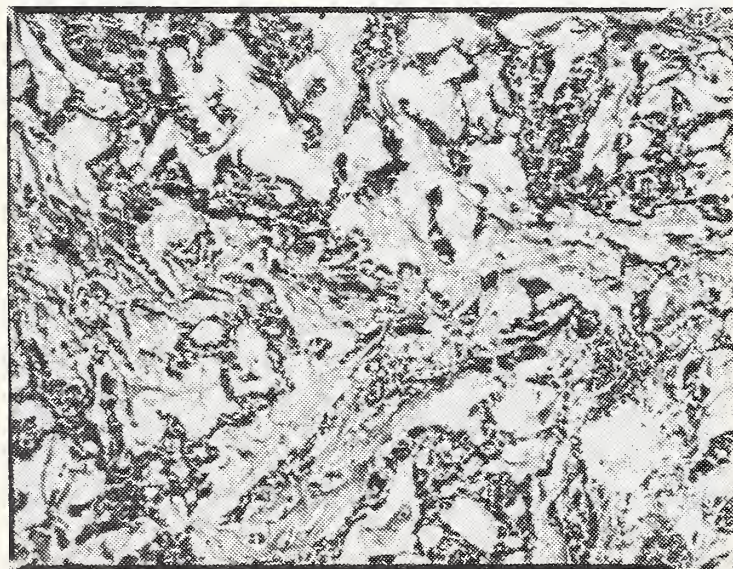


Fig. 2 — Histologic appearance of tumor mass found in mediastinum at autopsy. (X100 H & E)

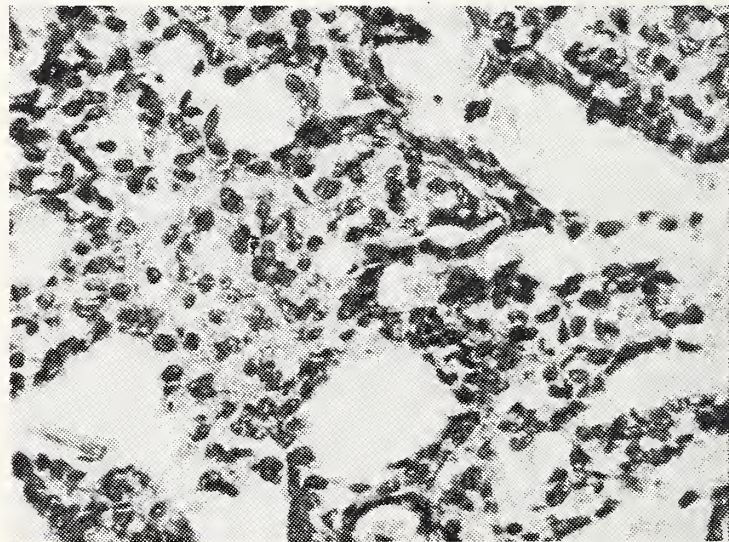


Fig. 3 — Primitive cords and ductlike structures are present, typical of embryonal carcinoma. (Hematoxylin and Eosin, X250 X 400).



epidemiologic terms, there is considerable prognostic difference between the two groups.<sup>9,10</sup> The mediastinal neoplasms of this type have a substantially less favorable outlook than their counterparts in the testes or ovaries. In particular, mediastinal embryonal carcinoma is associated with dismal survival statistics. In a study by Recondo and Libshitz, all patients with this diagnosis were dead within two years after the initiation of therapy.<sup>6</sup>

The likelihood is low that embryonal carcinomas of the mediastinum will be detected while small and potentially curable.<sup>6,9,10</sup> Even asymptomatic patients who have fortuitous detection of their neoplasms, as in this case report, usually have extensive tumor masses. The remaining cases manifest with symptoms referable to the displacement of mediastinal structures (cough, chest pain, superior vena caval syndrome) by the mass. The great majority of these individuals have incurable disease at the time of diagnosis, and 30 to 40% will already have clinically silent metastases.<sup>6,11</sup>

The histopathology of germ cell malignancies is of significant prognostic importance. In this instance, the presence of a small embryonal carcinomatous element in the original biopsy determined the ultimate fate of the patient, even though the majority of the neoplasm was seminomatous in appearance. In other words, a tumor composed of a mixture of germ cell elements assumes the prognosis of its most aggressive constituent.<sup>6</sup>

A note must be made of the potential functional nature of germ cell malignancies. Though the production of human chorionic gonadotrophin (HCG) is more frequently associated with choriocarcinoma, embryonal carcinomas may also produce this hormone. Gynecomastia and impotence in males, and menstrual irregularities in women represent the pathophysiologic effects of excessive HCG. Carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) may also be synthesized by embryonal carcinoma.<sup>12</sup> Any or all of these products can be used to screen for the recurrence of tumor in individuals who have received treatment, and who have been shown to have elevated levels of these substances prior to therapy. Their disappearance also provides an objective means of judging the effectiveness of ongoing treatment. The prognosis of patients in whom these products are found may not be as poor as was formerly thought.<sup>11-13</sup> Regrettably, neither HCG, CEA, nor AFP were measured in the present case.

The modalities currently used for the treatment of germ cell malignancies are often only palliative, and are far from innocuous. Though in the present

case, radiotherapy and chemotherapy confined the tumor to the thoracic cavity, they were not successful in eradicating neoplastic growth. Also, both modalities produced considerable pulmonary toxicity with resultant interstitial fibrosis and fibrous pleuritis. It is unfortunate that two of the drugs which are very effective against germ cell tumors (bleomycin and adriamycin) are also potential causes of treatment-related pulmonary fibrosis when given in conjunction with radiotherapy. Nonetheless, in instances of disseminated embryonal carcinoma, involving lymph nodes, bones, liver, and lungs, the aggressive use of these measures may offer the only hope for extended survival.<sup>14</sup>

### Summary

Germ cell tumors, including embryonal carcinoma, may arise as primary neoplasms in the mediastinum. They are most common in the third and fourth decades of life, and have a predilection for males. When present, symptoms are produced by a mass effect within the thorax. The prognosis of these lesions is worse than that of gonadal growths with identical histology. Mediastinal embryonal carcinomas may manufacture either HCG, CEA, or AFP. The treatment of these tumors has considerable attendant morbidity,

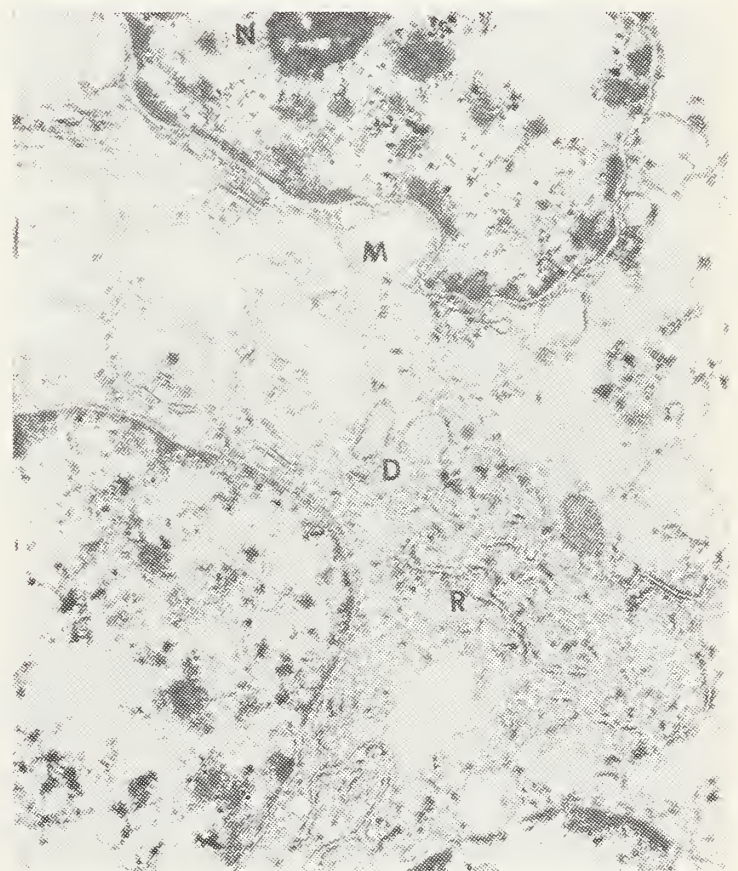


Fig. 4 — Electron micrograph of embryonal carcinoma tumor cells. Note prominent nucleoli (N), dilated mitochondria (M), rough endoplasmic reticulum (R), and desmosomes (D). (Uranyl acetate and lead citrate, X 7,000).



and even under the best therapeutic circumstances, a large number of patients die within two years after diagnosis.

#### Acknowledgment

The authors wish to express thanks to Dr. W. D. Edwards (Department of Pathology and Anatomy, Mayo Clinic) and to Dr. R. F. Morton (Division of Medical Oncology, Department of Internal Medicine, Mayo Clinic) for their critical review of this manuscript.

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#### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
3. Has made outstanding contributions to the Medical School, the University, the Alumni, and the community.
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Konald A. Prem, M.D., Chairman,  
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Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.

#### COVER PHOTOGRAPH

“Fall in the North Country”

Dr. George Crow, a family practitioner practicing in International Falls, took the cover photograph of Rainy Lake, ten miles East of International Falls, early in the Fall last year. A Voightlander 35 mm camera with a f2.8 lens was used. Camera setting was f 5.6 at 1/60 with a Kodak Kodacolor ASA 100 film.

Dr. Crow is a cofounder and member of the Falls Medical Center in International Falls and a graduate of the University of Minnesota Medical School. He and his wife, Lois, have three children, and the entire family enjoys the outdoors, fishing, boating, skiing, together.



# Hospice Care

## Care of the Dying/Hospice

ROBERT S BROWN, M.D.\*

*"The role of medicine is to cure sometimes, relieve often, comfort always."*

*Anonymous – 15th Century*

IT IS THE INTENT of this section to provide a forum to examine current approaches to the care of dying patients. The Hospice program of care for the dying patient is one approach which we will examine in detail over the next several months, but it is just one approach, and our intent is to cover a spectrum of approaches to caring for dying patients. We hope to avoid excessive time and energy wasted on semantics; i.e., "terminal," "end-stage disease," "palliative-care," etc., not that such discussion should not take place, but if we dealt only with this aspect, we shall fail our purpose: To improve the care of our dying patients.

### Definition of Hospice

A Hospice program of care means a centrally coordinated program providing for home and inpatient care for the patient-family unit experiencing a life threatening disease with a limited prognosis. This program uses an interdisciplinary team approach. Selected, adequately prepared and supported professional and/or lay volunteers are integral to the philosophy of care. The emphasis is on meeting the physical, psychosocial, and spiritual needs which may be experienced during the final stages of illness, dying, and the bereavement period. This care is available 24-hours a day, seven days a week.

Hospice as a program of care for the dying has developed because of a need within the health care system. There can be little argument that there would be no "Hospice movement" if the needs of the dying and their families were being met adequately. One is not saying that a Hospice program of care is needed by all dying patients. Nor is one ignoring the fact that many dying patients and their families have had their needs met adequately and well by the health care system long before "Hospice care" became synonymous with "care of the dying". There is little doubt that there has been an increased awareness of the needs of dying patients and their families over the past ten-to-fifteen years. Hospice as a program of care for the dying patient has enabled a focusing on the meeting of those needs.

The International Work Group in Death, Dying and

Bereavement is quoted: "There is agreement that patients with life-threatening illnesses, including progressive malignancies, need appropriate therapy and treatment throughout the course of illness. At one stage, therapy is directed toward investigation and intervention in order to control and/or cure such illness and alleviate associated symptoms. For some persons, however, the time comes when cure and remission are beyond the capacity of curative treatment. It is then that the intervention must shift to palliative care, which is designed to control pain in the broadest sense and provide personal support for the patient and family during the terminal phase of illness. In general, palliative care requires limited use of apparatus and technology, extensive and intensive personal care, and an ordering of the physical and social environment to be therapeutic in itself."<sup>1</sup>

The use of any therapy must be appropriate. For the cancer patient, radiation and chemotherapy can still be appropriate for symptom control when they are no longer appropriate for cure or prolongation of life. Thus, although there may be much less emphasis on the technological aspects of medicine in a Hospice program, this does not mean that one abandons quality medical care. Diabetic and cardiac patients require close monitoring of their medications. The occasional patient will need intravenous fluids or blood transfusions. Always the emphasis is on relief of symptoms and providing a quality of life rather than a prolongation of life. Hospice is not just tender, loving care, but efficient, quality medical care.

"Hospice programs are not anti-therapy or anti-physician. Hospice utilizes the specialized skills and knowledge of physicians and retains overall physician supervision of medical care. Hospice requires a high degree of skilled professional services to provide broadly defined symptom control and therapy appropriate to the patient's needs. Hospice differs, however, from traditional care of the dying in its reliance on an inter-disciplinary team effort that uses the services of social workers, clergy, home health aides, pharmacists, volunteers and others, in addition to physicians and nurses. Further, the hospice philosophy stresses improved coordination and continuity of care with

\*St. Paul, Minnesota.



## CARE OF THE DYING/HOSPICE

utilization, whenever possible, of existing community resources."<sup>2</sup>

In the months ahead we will be considering some of the following topics and issues as we focus on the care

of dying: home care, symptom control, patient-physician attitudes, bereavement, standards, accreditation, reimbursement, licensure, the dying child, the family, and staff support, among others.

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### MMA Cosponsorship Program

Institutions and organizations seeking MMA cosponsorship for their CME programs (for AMA or LCCME Category 1 credit) may obtain information and application forms from:

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Minnesota specialty societies that are represented on the MMA Interspecialty Council and have already appointed "CME Coordinators" to work with the MMA in cosponsorship relationships should have their coordinators submit application for cosponsorship at least *30 days* in advance of the program date.

Other groups may be assigned an MMA representative as "CME Coordinator" upon approval by the MMA Subcommittee on CME Resources. This representative will participate in the planning process in order to assure that the criteria for Category 1 credit are met and will subsequently submit the application for cosponsorship. Request for a cosponsorship representative must be made at least *90 days* in advance of the program date.

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# Rheumatology Corner

## Reiter's Syndrome

DAN HATHAWAY, M.D.\*

Reiter's Syndrome is a disease of unproven etiology which is classically characterized by the triad of arthritis, nongonococcal urethritis and conjunctivitis. To this triad should be added skin and mucous membrane lesions. Although the etiology is unproven, Reiter's Syndrome is classified as a reactive arthritis. This means the syndrome typically follows an infection by a period varying from days to one month. The infections most definitely implicated have been diarrheal illnesses caused by *Salmonella typhimurium*, *Shigella flexneri*, *Yersinia enterocolitica* and *Campylobacter fetus*. In the United States, Reiter's Syndrome more commonly follows venereal exposure than diarrhea, and the suspected bacterial stimulus is *Chlamydia*. Approximately 90% of patients with Reiter's Syndrome carry the B27 histocompatibility antigen. The prevailing theory, therefore, is that some patients with this genetic marker have a predisposition to develop Reiter's Syndrome when exposed to a variety of bacterial antigens. The manifestation of the disease is secondary to an immunologic response to the antigen and not directly related to the infection. Thus one is unable to culture the organisms from the involved joints.

Epidemiologically, in the United States, Reiter's Syndrome is most commonly diagnosed in sexually active young men. The disease does occur in both women and children, but more commonly follows an episode of diarrhea. There is some controversy as to the frequency of Reiter's Syndrome in women with the impression that perhaps it is underdiagnosed because they do not develop the complete triad of symptoms.

Clinically, the arthritis is typical of the rheumatoid variants. It is asymmetrical and tends to involve the lower extremities. Statistically, the most involved joints are the knees, then ankles and MTPs. Interphalangeal joint involvement in the toes is less common but very characteristic, giving the sausage-toe appearance. As with the other rheumatoid variants, sacroiliitis and spondylitis can occur both early and late in the disease. The patients frequently have tendonitis and periostitis, especially around the heel, manifested as Achilles tendonitis, plantar fasciitis or simply pain upon squeezing the calcaneus. The urethritis can vary from an asymptomatic watery discharge to pus with dysuria. Inflammation of other portions of the genitourinary tract can also be seen. If the disease presents with diarrhea, this can also be of varying severity, from mild to an illness resembling inflammatory bowel disease. The most typical eye involve-

ment is painless conjunctivitis, but more serious forms of anterior uveitis can occur. Mucous membrane lesions include painless ulcerations on the penis, tongue or buccal mucosa. Skin lesions include painless hyperkeratotic pustules. They are typically on the palms and soles, but can occur elsewhere on the body. Histologically, they are indistinguishable from pustular psoriasis. Hyperkeratotic finger and toenail involvement are also indistinguishable from psoriatic or fungal disease. An occasional patient will be constitutionally ill with fever, sweats and weight loss.

Reiter's Syndrome has classically been considered a self-limited disease lasting from six weeks to six months. Recently, there has been controversy in the literature suggesting that many patients with Reiter's Syndrome will manifest some chronic disability. This could be chronic peripheral arthritis, sacroiliitis and spondylitis, or chronic uveitis.

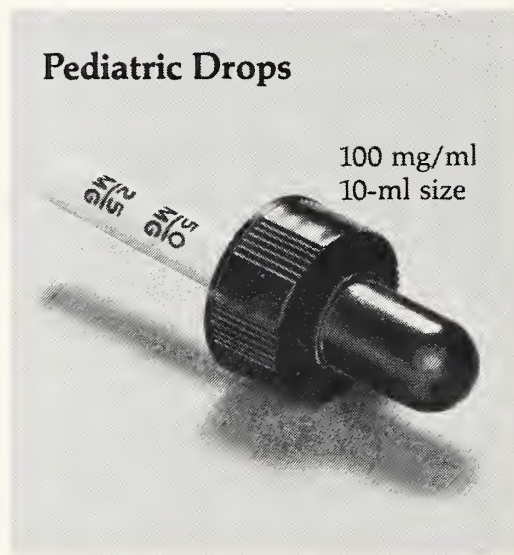
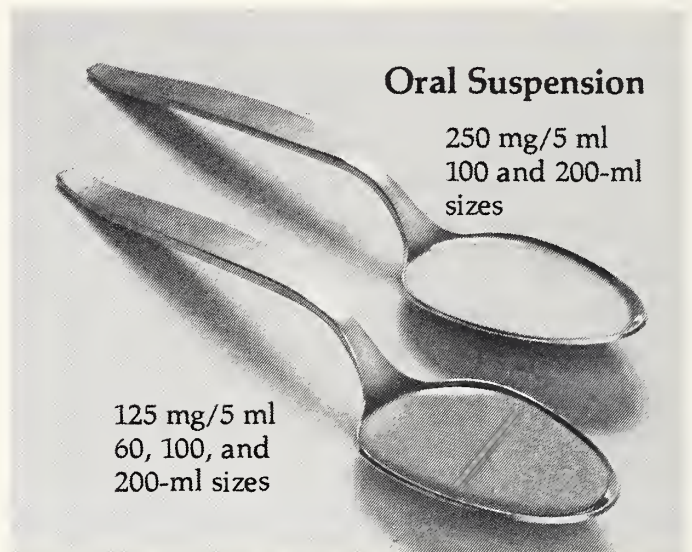
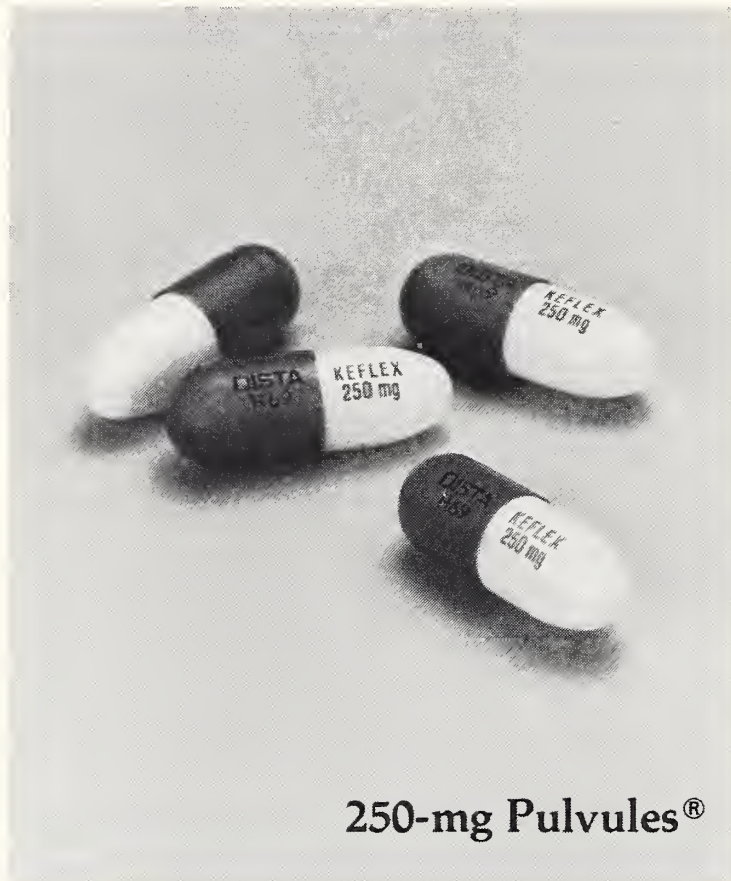
The laboratory is of little help in making the diagnosis of Reiter's Syndrome. The urethral discharge should be cultured, but even if gonococci should be documented, the patient can still concomitantly develop Reiter's Syndrome. Sedimentation rates are commonly, but nonspecifically, elevated. Synovial fluid analysis early will demonstrate between 2,000 and 50,000 or more white blood cells, most of which would be PMNs. Synovial fluid complement is typically normal or even elevated. As mentioned earlier, a high percentage of these patients are B27 positive.

Obviously, gonorrhea requires treatment if it is documented. Although tetracycline is commonly used for the nonspecific urethritis, there is no proof of benefit for the other manifestations of Reiter's Syndrome. Despite this, it is not unusual or unacceptable to treat the patient with a course of tetracycline in an attempt to eliminate the bacterial antigen, especially if the patient is having recurrent attacks. The promiscuous male should be advised to use condoms. The nonaspirin, nonsteroidal antiinflammatory drugs tend to be most efficacious in the treatment of the arthritis. Examples would be Indocin in dosages up to 200 mg. per day, Tolectin 400 mg. tid, or Clinoril 200 mg. bid. If one or two joints persist in causing the patient significant disability, an intraarticular injection of triamcinolone hexacetonide may be beneficial. Patients who do not respond to these forms of therapy or go on to chronic disability should be referred for evaluation by an internist interested in rheumatic diseases or a rheumatologist.

\*St. Paul Ramsey Medical Center, St. Paul, Minnesota.



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# Pregnancy Termination

## Choriocarcinoma Presenting as a Complication of Elective First Trimester Abortion

FRED A. LYON, M.D.\* and LEON L. ADCOCK, M.D.\*

A case of choriocarcinoma is reported which was detected two weeks following elective termination of pregnancy. The original pathology report of the material obtained at the time of the abortion stated that "products of conception" were present as well as "decidual cast, placental membrane and degenerating trophoblast".

At the post-abortion examination a pelvic mass was found and the pregnancy test was still positive. At laparotomy malignant trophoblast was present on the serosal surface of the uterus at the site of a spontaneous perforation. Histologic review of the original endometrial contents showed "hydatidiform mole with one area of myometrial invasion".

All material obtained at the time of elective first trimester abortion must be thoroughly examined and patients strongly advised to seek post-abortion care. Pathologists must describe the microscopic findings of tissue submitted and not submit reports with gross diagnoses such as "products of conception". The presence or absence of normal chorionic villi must be established if accurate diagnoses are to be made and tragedies avoided.

**E**LECTIVE PREGNANCY termination is one of the most frequently performed surgical procedures in the United States. It has been estimated that more than one million abortions are performed annually.<sup>1</sup> It is imperative that physicians performing abortions or providing post abortal care for such patients recognize certain serious complications if possible tragedies are to be averted. A potentially more serious situation has recently been observed and is presented here, in which metastatic gestational trophoblastic disease was detected at a routine two week post-abortion examination.

### Case Report

An eighteen-year-old, unmarried, white, gravida 1, para 0 patient presented herself to a free-standing, out-patient abortion facility for an elective first trimester abortion on March 31, 1978. She had been examined by another physician on March 24, 1978. The referral note stated that a urine pregnancy test was positive and that the uterine corpus was six weeks' gestational size. The patient was unsure of the exact date of her last menstrual period. She has been using an oral contraceptive medication but had ceased taking it sometime in late February, 1978. She began to bleed daily thereafter. At the beginning of March, 1978 bleeding increased and she passed several large blood clots. She also experienced chills and fever.

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Reprint Requests: Fred A. Lyon, M.D., Medical Director, Meadowbrook Women's Clinic, 6490 Excelsior Boulevard, St. Louis Park, Minnesota, 55426.

On examination, the day of the scheduled vacuum abortion, the patient appeared pale but was otherwise healthy. Her temperature was 37°C. Her hemoglobin was 9.2 gms. %. The corpus was enlarged and retroverted. Bilateral ovarian enlargement was present. Following a 1% Lidocaine paracervical block, the uterus was sounded to 11.0 cm. The cervical canal was dilated to a number 39 Pratt. There was almost no resistance present at the internal cervical os. The uterine contents were coarse and irregular and only a scant amount of tissue was aspirated. Neither chorionic villi, vesicles, nor placental tissue were detected on gross examination of the uterine contents. It was the impression of the operator that the most likely diagnosis was incomplete abortion.

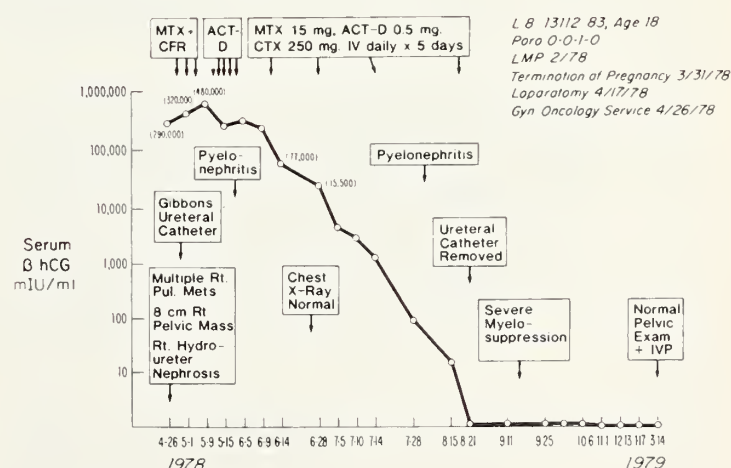


Figure — Course of Beta-sub-unit HCG during Chemotherapy for Choriocarcinoma.



The removed tissue was submitted for pathologic evaluation. The patient was given an oral contraceptive medication as well as oral iron to treat the existing anemia. She was given an appointment for a two week post-abortion examination.

On April 14, 1978 a right adnexal mass was present measuring 7 by 8 cm. The uterine corpus was retroverted and of normal size. A urine pregnancy test was positive. The pathology report of March 31, 1978 noted "the presence of a decidual cast, placental membrane and degenerating trophoblastic tissue. There is no evidence of malignancy". The conclusion was "Products of conception".

The patient was admitted to a Metropolitan Hospital. Her temperature was 37.6°C. Her hemoglobin was 9.5 gms. % despite two weeks of oral iron therapy. Examination under general anesthesia showed the uterine corpus to be retroverted and of normal size. A right adnexal mass was fixed in the pelvis. Reaspiration and curettage of the uterine cavity produced minimal tissue. A diagnostic laparoscopy found a nodular adnexal mass adherent in the right pelvis.

A laparotomy was performed. The broad ligaments contained large varices. Both fallopian tubes were red and edematous. Purulent material drained from the mid portion of the left tube. The right adnexa was densely adherent to the cul-de-sac and the posterior leaf of the broad ligament. Adhesions were lysed and cultures taken. In the process of dissecting the right adnexal mass, profuse hemorrhage occurred. It became apparent that a perforation existed in the right posterior uterine wall to which the adnexal mass was adherent. Biopsies were taken of the uterine serosa at the site of the perforation. Sutures controlled the bleeding. The appendix was removed and the surgical procedure terminated. Transfusions of whole blood were given.

Microscopic review of the uterine curettings showed several large chorionic villi with hydropic changes and isolated clumps of active trophoblastic tissue with atypical features. Biopsy material of the serosal uterine surface at the site of the perforation showed "sheets of bizarre syncytiotrophoblastic tissue".

The patient recovered after a stormy post-operative course complicated by paralytic ileus and fever. Although a chest radiogram on admission was normal, after surgery an infiltrate or atelectasis was present in the left base. A follow-up chest radiogram showed an increase in the lower lobe infiltrate.

The patient was transferred to the Gynecologic Oncology Service of the Department of Obstetrics and Gynecology at the University of Minnesota Hospitals with a diagnosis of metastatic trophoblastic disease. On admission the patient was asymptomatic. The uterine corpus was slightly enlarged and deviated to the left by a hard, fixed, tender, eight centimeter mass between the right pelvic wall and the corpus.

Laboratory evaluation was normal with the exception of a creatinine clearance of 61 ml./minute. A chest radiogram showed nodular densities in the right upper lobe and right costo-phrenic angle confirmed by full lung tomography. An intravenous pyelogram showed only a right nephrogram at seven hours. Liver and brain scans were normal. A right retrograde pyelogram found an obstruction of the right ureter with marked hydronephrosis and hydronephrosis. A Gibbons catheter was placed. The patient was treated with an eight day course of alternating daily doses of intramuscular Methotrexate and Citrovorum factor rescue. Dosages were reduced during the final four days of treatment because of a rise in the SGOT to 50 units. The serum beta sub-unit hCG level was 320,000 m.I.U./ml. Actinomycin-D was then given intravenously for five days and the patient was discharged.

The patient was re-admitted two weeks later because of severe right flank pain secondary to right ureteral obstruction. The Gibbons

catheter was inserted into the right renal pelvis. The serum beta sub-unit hCG level had risen to 480,000 m.I.U./ml. She was then treated with a five day course of intravenous Actinomycin-D, Methotrexate and Cytosan. Two weeks later the serum beta (hCG) level was 77,000 m.I.U./ml.

Two weeks later the patient returned for the second five day course of triple chemotherapy. A chest radiogram showed a total disappearance of the pulmonary nodules. The serum beta sub-unit hCG level was 15,500 m.I.U./ml. The pelvic mass had decreased in size.

After two weeks a third course of triple chemotherapy was given. On August 9, 1978 the patient was re-admitted with right flank pain, fever and a fifteen pound weight loss. The pelvic mass was now 4 cm. in diameter. The hemoglobin was 8.8 gms. % and the white blood count was 2,500. A chest radiogram was normal. The marked dilatation of the right upper urinary collecting system was unchanged from the previous examinations. The urinary tract infection was successfully treated with antibiotics and a fourth five day course of triple chemotherapy was given.

The Gibbons ureteral catheter was removed on August 18, 1978 and withdrawal ureterogram showed only moderate delayed drainage of the right collecting system. The serum beta sub-unit hCG level on August 21, 1978 was normal and has remained so.

On September 8, 1978 the fifth five day course of triple chemotherapy was begun. On September 20, 1978 the patient was re-admitted with a temperature of 39.4°C and pharyngitis. Her hemoglobin was 8.4 gms.%, the white blood count was less than 1,000 and the platelet count was 68,000. The fixed 4 cm., right pelvic mass was unchanged. She responded rapidly to antibiotic therapy.

Subsequently the patient has been asymptomatic and has gained twenty-five pounds. The serum beta sub-unit hCG determinations have all been normal. Pelvic examinations have been normal. An intravenous pyelogram shows only moderate dilatation of the right upper urinary collecting system. She is currently using oral contraceptive medication. Her course is illustrated in the Figure.

## Discussion

Hydatidiform mole and choriocarcinoma are rare occurrences in routine obstetrical practice. The incidence of molar pregnancy is said to be one in every 1,200 to 2,000 pregnancies in the United States. Choriocarcinoma is even more rare. It follows as a malignant sequela in approximately three per cent of patients with a hydatidiform mole. It may rarely occur following a normal term pregnancy or a spontaneous abortion. In its metastatic form it was formerly the most uniformly and rapidly fatal malignancy in women. It has now become the one solid malignancy that can be cured with chemotherapy.<sup>2</sup> Normal subsequent pregnancies are possible and have been reported.<sup>4</sup>

It is imperative that all tissue removed by aspiration or curettage during an elective abortion be carefully examined. Whether all such tissue should be examined microscopically is still being debated. The presence of normal placental tissue must be verified. A number of early hydatidiform moles have been detected by an examination of the conceptions in our clinic. These patients were notified to seek proper follow-up care.



Serial hCG determinations are mandatory in such cases to insure that gestational trophoblastic disease does not persist. These patients must be encouraged to use reliable contraception to prevent future pregnancies for a period of one year.

Should chorionic villi not be detected on gross examination of the aspirated and curetted material the tissue must be submitted for histologic examination. Should villous structures not be seen microscopically the patient must be immediately contacted and urged to seek appropriate medical care. The diagnosis of ectopic gestation must be excluded.<sup>3</sup>

The pathologist evaluating the products of conception from a patient following an elective pregnancy termination must be alerted to carefully examine all of the submitted tissue. Significant abnormalities such as hydropic molar changes must be recognized. A report of "products of conception" is not sufficient. Villi of normal pregnancy must be identified and reported to the operating physician.

A retrospective review of the microscopic sections of the material initially removed by the vacuum curettage reported actually showed tissue diagnostic of hydatidiform mole, grade II, with one area of myometrial invasion. Had this information been available to the responsible clinician when the patient returned for the two week post-abortion examination,

coupled with a persistently positive pregnancy test, the diagnosis of gestational trophoblastic disease would have been evident. Such information would have avoided the laparotomy required to make the diagnosis.

Fortunately, the correct diagnosis became apparent when the uterine perforation was recognized at surgery as choriocarcinomatous perforation of the myometrium. Had the diagnosis not been recognized, total abdominal hysterectomy and bilateral salpingo-oophorectomy may well have been performed. No future childbearing would then have been possible for this young woman.

Patients who have had elective terminations of pregnancy should be strongly urged to seek post-abortion care. Urinary pregnancy tests should be performed routinely at the time of the post-abortion examinations. A positive pregnancy test should alert the physician to the possibility that the pregnancy was not successfully terminated. An ectopic tubal pregnancy may be present or the intra-uterine pregnancy may still be viable. A combined intra and extra-uterine pregnancy may have been present. If both of these conditions are ruled out, the physician must begin an immediate evaluation to make certain that gestational trophoblastic disease is not present.

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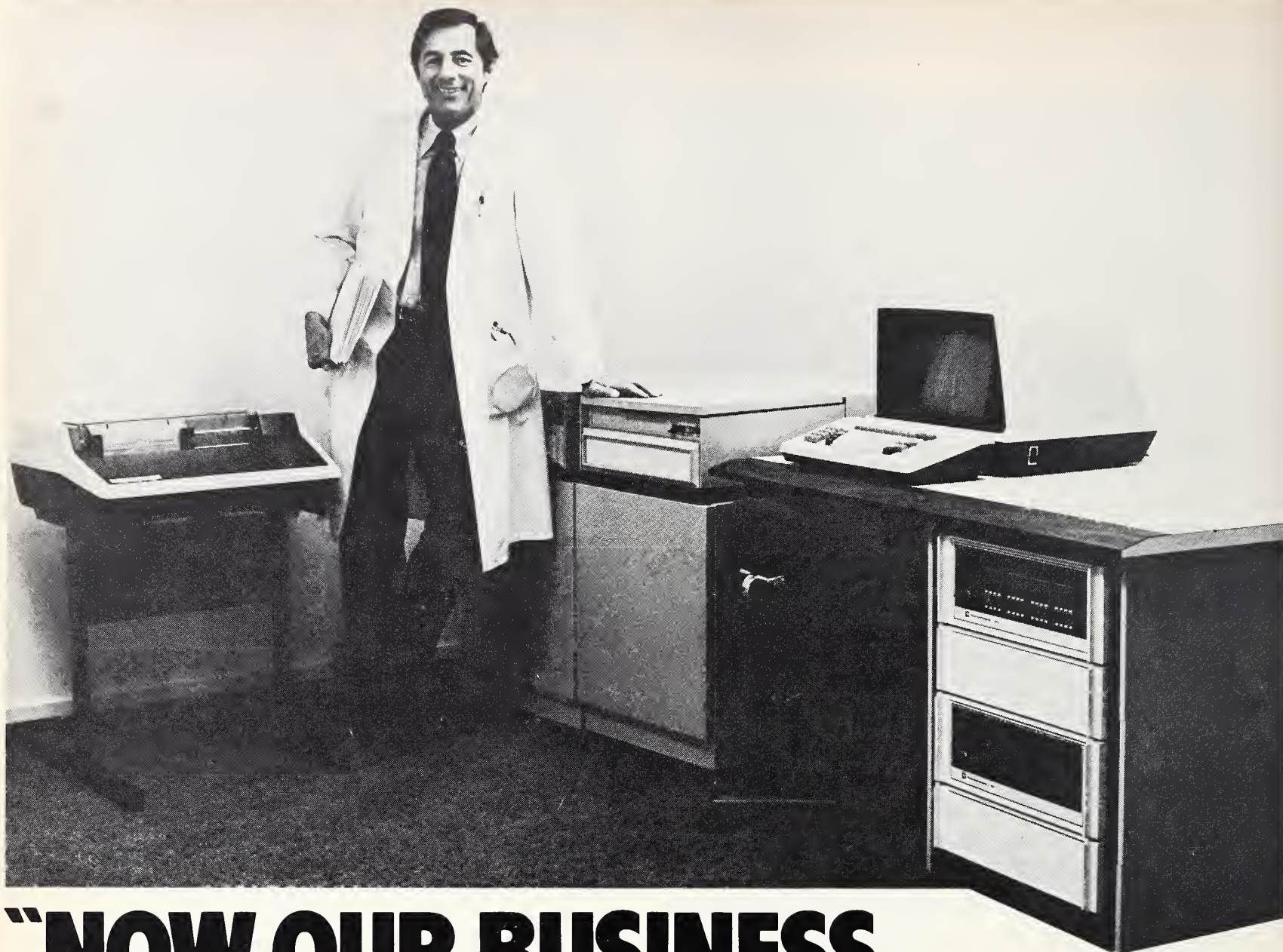
#### Continuing Medical Education St. Paul-Ramsey Medical Center

The fourth *Clinical Toxicology* Quarterly Update Conference will be held in The Gillette Amphitheater at St. Paul-Ramsey Medical Center on Wednesday, November 12, 1980. Speaker will be Dr. Anthony R. Temple, Director of Medical Affairs, McNeil Consumer Products. Subject of his talk will be "Iron Poisoning". Conferences qualify for Category I CME credits. Sponsored by the Emergency Medicine Department at St. Paul-Ramsey Medical Center and the University of Minnesota Medical School under the direction of Dr. Kusum Saxena. For further information please contact: Carol J. Wolf at (612) 221-3311.

#### Vail, Colorado: Medical Education Symposium

"Management of Common Office Problems", January 18, 19, 20, 1981, 4 hours/day, Approved for Category I. For Brochure write: Medical Education Dept., St. Luke's Hospital, 915 East First Street, Duluth, Minnesota 55805.





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# Fracture Conference

## Elbow Injuries

WILLIAM P. COONEY III, M.D.\*; MICHAEL J. MORRISON, M.D.†; WILLIAM V. WATSON, M.D.†;  
and MIGUEL E. CABANELA, M.D.\*

**Dr. William P. Cooney III:** Elbow fractures and dislocations will be discussed in this fracture conference.

### Case 1

**Dr. Michael J. Morrison:** A 63-year-old white woman fell off a step stool and landed on her extended right arm. A fracture dislocation of the elbow was diagnosed. The dislocation was reduced, and she was referred to the Mayo Clinic (Figure 1(A) and (B)).

**Dr. Mark P. Brodersen:** A small chip of bone can be seen over the lateral epicondyle, and the capitellum may be injured. The lateral view shows a chip of bone from the radial head. The location is indefinite, but it appears to be a fracture of the radial head.

**Dr. Morrison:** The patient had considerable pain over the lateral aspect of her elbow, and her range of active motion was limited to 30°.

**Dr. Brodersen:** Because she probably would have much pain if the fragments were left in the joint, I would recommend surgical removal of the fragments.

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†Resident in Orthopedics, Mayo Graduate School of Medicine (University of Minnesota), Rochester, Minnesota.

Fracture Conference, April 27, 1977.

**Dr. Morrison:** At the time, because we wanted to determine the number of fragments involved and the amount of radial head surface involved, we obtained a tomogram (Figure 1 (C)).

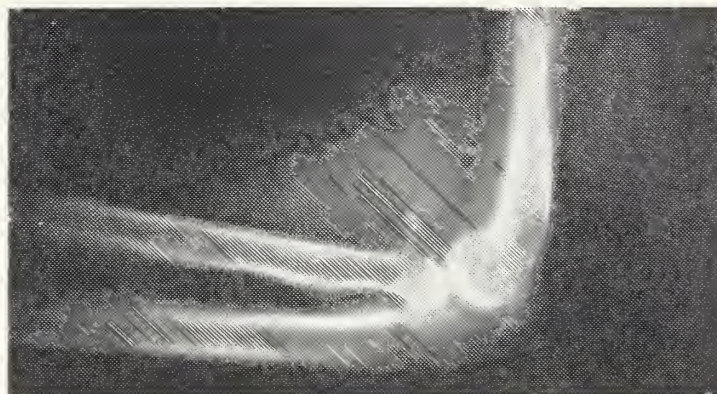


Fig. 1(C) — Lateral tomogram shows that major portion of radial head is not involved and that less than one-third of the articular surface is affected.

**Dr. Cooney:** What are the criteria for the decision on the treatment of this radial head fracture?

**Dr. Brodersen:** If more than half of the radial head is involved, the fragments should be removed.

**Dr. Cooney:** Is the treatment different if the elbow is dislocated and if the patient tends to sublux in 45° flexion?

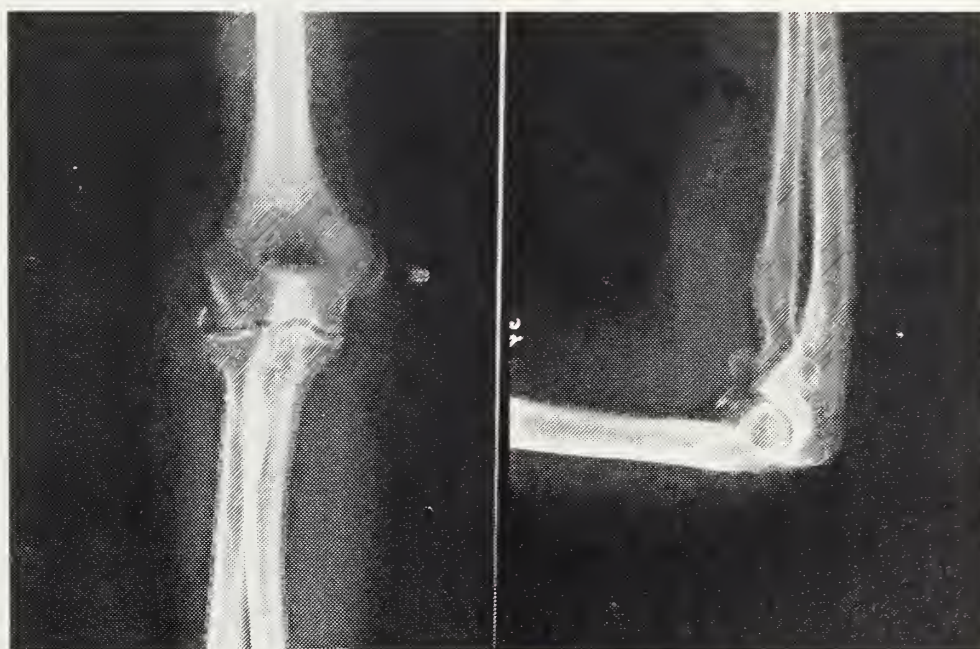


Fig. 1 — (Case 1). Original anteroposterior (A-left) and lateral (B-right) views of right elbow showing that elbow is reduced and that radial head is fractured. Anteroposterior view reveals that fragment is displaced laterally. Lateral view shows several fragments of radial head fracture.



**Dr. Michael R. Wilson:** Yes. The standard rules for radial head excision are: (1) compression of 3 mm or more, (2) angulation greater than 30°, and (3) involvement of more than one-third of the radial head. In radial head fractures in the presence of true elbow dislocation, the radial head should be left attached unless severely comminuted, because it provides lateral stability. A Silastic prosthesis to replace the radial head should be considered in comminuted fractures. I would be inclined to agree with Dr. Brodersen and attempt an open reduction and fixation of the radial head fragments, unless the previously mentioned criteria were not met.

**Dr. Morrison:** The decision was made to remove the fragments of the radial head. Less than one-third of the head was involved.

**Dr. Mark B. Coventry:** Where did the fragments come from? Was the capitellum the source of the fragments or were the fragments all from the radial head?

**Dr. Morrison:** The fragments were all from the radial head; the capitellum was not involved.

**Dr. Thomas C. Shives:** How long after the dislocation was the operation done?

**Dr. Morrison:** The patient was seen a few hours after the fracture, but the operation was delayed 48 hours.

**Dr. Shives:** If treatment had to be performed, I thought that it either should be done during the first 24 hours or delayed a few weeks or even months.

**Dr. Cooney:** How many weeks would you wait?

**Dr. Shives:** I think two to three months would be adequate.

**Dr. Cooney:** What do you base your decision on?

**Dr. Shives:** You can wait and find out if the patient regains functional motion. The literature suggests that, if you try to operate on these patients in the interim between the immediate fracture period and the later date, the chances for myositis developing may be increased.

**Dr. Cooney:** Charnley stated that you should wait two weeks, put the patient through range of motion, and then determine whether the elbow is stable or the radial head fracture interferes with motion. If there is interference with motion, the fracture should be excised. Most other people, though, probably would agree with Dr. Shives. But rather than 24 hours, a period of 48 to 72 hours is more acceptable. With an associated dislocation, the radial head fracture probably should be treated independently of the dislocation as long as instability of the elbow does not result.

Because we weren't sure how much of the head was involved, we obtained tomograms. These revealed that about one-third of the radial head was involved on the medial side; therefore, we thought that the fragments should be removed.

**Dr. Richard S. Bryan:** Statements in the literature are predicated on retrospective studies, and most of those retrospective studies involve various surgical skills. The amount of damage is influenced by the skill of the surgeon. The less skilled the surgeon, the more damage and the more myositis ossificans.

**Dr. Robert D. Beckenbaugh:** What did you advise this patient about the prognosis at the time that you wanted to excise the radial head?

**Dr. Cooney:** What would you advise them?

**Dr. Beckenbaugh:** There is a significant chance that bone will form about the elbow, with or without an operation, and this bone may cause considerable stiffness and the loss of elbow motion. These patients should be told that this sometimes is an unavoidable complication and that there would be more problems with the elbow itself than with the radial head fracture.

**Dr. Cooney:** This point is particularly pertinent



Fig. 1(D) — Final anteroposterior roentgenogram with range of flexion (125°) and extension (15°).



because the patient had an elbow dislocation. In four to six weeks, anterior calcification developed within the capsule and probably also in the brachialis muscle, which was torn in the dislocation process.

**Dr. Shives:** What range of motion did this patient have?

**Dr. Morrison:** The elbow was held in 90° and then allowed full flexion, with gentle extension from 90 to 45°. At five weeks she had 15° to 125° of flexion (Figure 1 (D)). At 10 days, we started allowing her full flexion and gradual extension from 90°.

**Dr. Cooney:** The use of early elbow motion was based on the concept that the elbow has a fixed center of rotation and that the elbow can be expected to move as a hinge-type joint. This hinge joint action can be provided by using an Orthoplast splint and having an outside hinge at the elbow. Motion is started earlier, in about seven to 10 days, using this hinge joint principle. The question whether motion should be early or late is debatable. The presence of dislocation should be a factor in this decision. But in general I think early motion is preferable. Dr. Bryan, do you agree with that?

**Dr. Bryan:** Yes. I think that early motion is very important. If you wait until the initial reaction subsides before you start motion, you often see more fibrosis and myositis, with a resulting loss of motion.

## Case 2

**Dr. Morrison:** A 54-year-old man fell on his outstretched hand, suffering immediate pain over the lateral aspect of the left elbow (Figure 2 (A)).

**Dr. Thomas E. Kaiser:** There is a bony fragment off the radial head and a fracture of the base of the radial head, with dorsal angulation of the proximal fragment.

**Dr. Morrison:** What are some of the considerations in treating this injury?

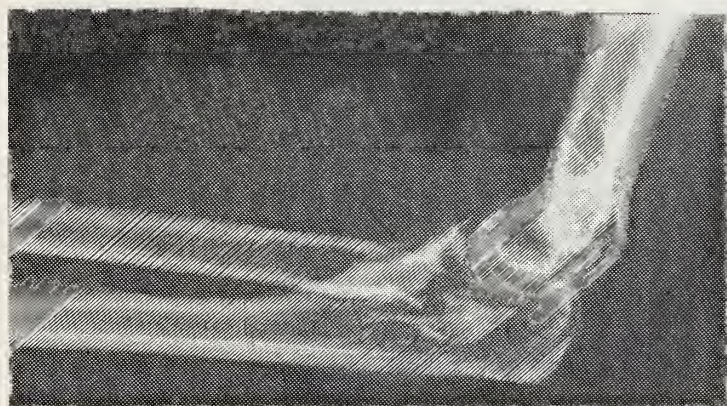


Fig. 2(A) — (Case 2) — Lateral view of left elbow shows fracture (long arrow) through radial neck as well as comminuted displaced fracture of radial head. Short arrows show displaced inferior fragment.

**Dr. Kaiser:** The decision is between conservative treatment with early motion and resection of the radial head with prosthetic replacement.

**Dr. Morrison:** Dr. Beckenbaugh, the patient had 80° of supination and pronation and no evidence of mechanical block or crepitus. How would this affect your thinking regarding treatment?

**Dr. Beckenbaugh:** I would not resect the radial head as long as nearly full motion is present because a loss of motion could result from surgical intervention.

**Dr. Morrison:** The radial head fracture had the fragment rotated. The radial head was resected, and a prosthesis was inserted (Figure 2 (B)). Four weeks

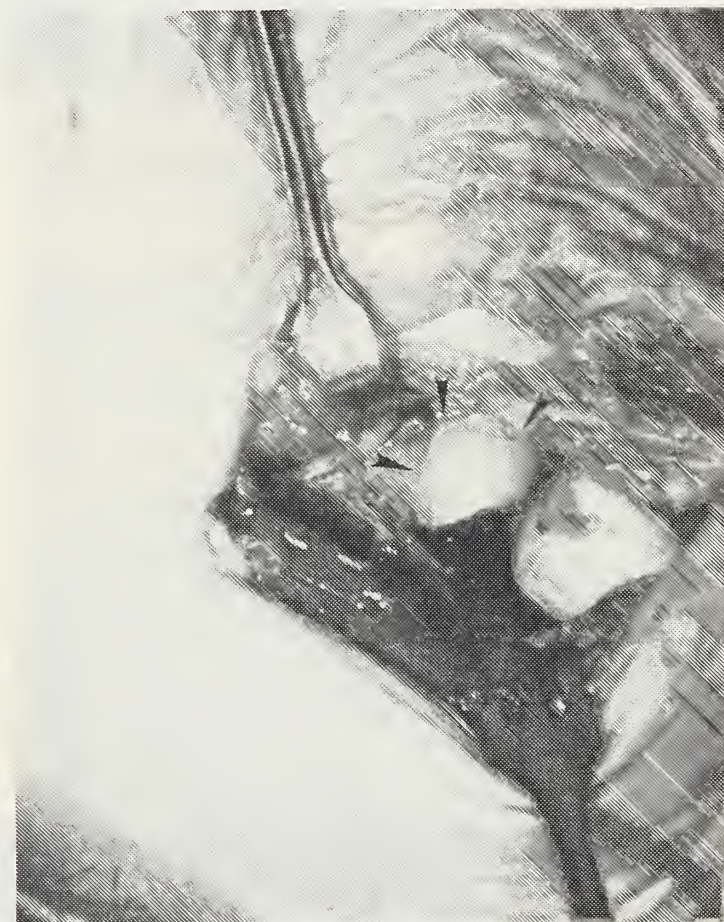


Fig. 2(B) — Operative view of radial head fracture through modified Kocher incision. Fracture fragment is displaced posteriorly (arrowheads). After the fragment was pushed anteriorly it was extracted from elbow joint.

after the procedure, the patient had 20 to 135° of flexion and full pronation, but he could supinate only 45°. He was seen again one year later, at which time he had full extension, flexion, supination, and pronation (Figures 2 (C) and (D)).

**Dr. Cooney:** Dr. Dobyns, do you consider the use of a radial head prosthesis after radial head excision?

**Dr. James H. Dobyns:** Not anymore. I have used a few. The last one I put in was in a young fellow and he did well enough until it dislocated about two years later from a particularly heavy torque stress at his work. I



had to take the prosthesis out. I do not believe that they are indicated.

**Dr. Cooney:** At our institution, 20 patients who had radial head excisions were reevaluated at the biomechanics laboratory. Most of the patients had had excision more than 5 years before, with an average of about 10 years. Despite that period of time, there was no proximal migration of the radius toward the capitellum. Despite the compressive forces associated across the forearm and elbow with lifting, the interosseous membrane was strong enough to prevent proximal migration. Thus, if there is proximal migration, and particularly if this is apparent on the original roentgenogram, then both the radial head and the interosseous membrane have been injured, possibly along with the distal radioulnar joint — the so-called Essex-Lopresti injury.

**Dr. Dobyns:** How could you distinguish this injury with proximal migration from an isolated radial head fracture?

**Dr. Cooney:** The differentiation could be made if there were symptoms of pain and discomfort at the distal radioulnar joint on physical examination or if there was actually a dislocation of the distal radioulnar joint.

**Dr. Coventry:** If there is a chance of proximal migration, would that change your mind about using a prosthesis?

**Dr. Cooney:** Yes. I would put in a prosthesis to help prevent this migration. We don't know how much force is borne by the radiocapitellar joint, but it has been estimated that about 40% of the forces of the elbow in flexion is borne by the capitellum. With

extension, the olecranon bears most of the elbow forces.

**Dr. Dobyns:** Which is the best prosthetic material: polyethylene or Silastic?

**Dr. Cooney:** Dr. Coventry, would you like to comment on the use of polyethylene?

**Dr. Coventry:** The only two reliable studies that I know of did not demonstrate that polyethylene against normal cartilage is bothersome. It probably is not, but we cannot assume that cartilage in the capitellum is going to be normal after an injury like this. Polyethylene probably should not be used unless there is nothing else. I do not know of any study that has evaluated Silastic against either roughened cartilage or exposed bone.

### Case 3

**Dr. Morrison:** A 75-year-old white woman fell down the steps, striking the posterior aspect of her right elbow (Figure 3 (A) and (B)).

**Dr. William K. Harryman III:** There is a transverse fracture across the olecranon and a radial head fracture: it is a fracture-dislocation.

**Dr. Cooney:** How would you treat this?

**Dr. Harryman:** This fracture-dislocation requires open reduction.

**Dr. Cooney:** What are the alternatives?

**Dr. Harryman:** Closed reduction could be done by holding the elbow in extension, but this probably would not be adequate.

**Dr. Cooney:** What are the problems if the elbow is put in extension?



Figs. 2 (C-left) and (D-right) — Roentgenograms taken more than 12 months after operation show that radial head prosthesis is well reduced and stabilized by lateral new bone formation.



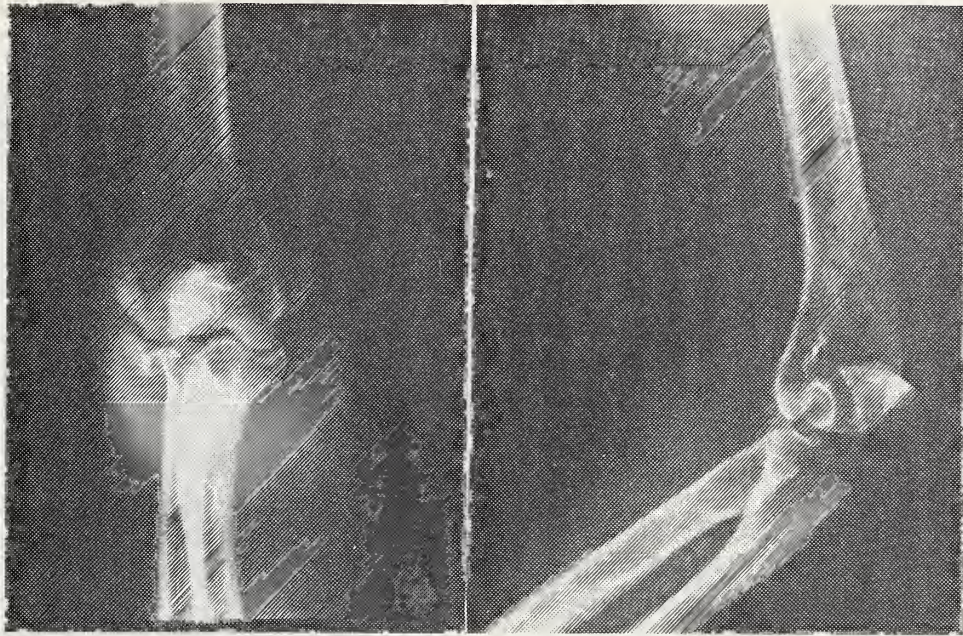


Fig. 3 (Case 3) (A-left) — Anteroposterior and (B-right) — lateral views of right elbow. Comminuted fracture of right radial head and displaced fracture of right olecranon associated with elbow dislocation.

**Dr. Harryman:** There is a problem of fracture alignment and joint congruity.

**Dr. Cooney:** What would happen to the triceps muscle in extension?

**Dr. Harryman:** The triceps muscle is relaxed, and this would allow approximation of the fracture fragments.

**Dr. Cooney:** If the reduction is treated closed and the elbow is put in extension, are there any problems with the other part of the injury?

**Dr. Harryman:** I think that the radial head is broken completely off, and I do not believe that you can satisfactorily reduce it and preserve elbow motion. So the decision involves excision of the radial head. In this case, the head probably should be excised. The olecranon fracture can be treated closed, can be excised, or can be treated open and fixed. I think that the fracture should be reduced and internally fixed with a long screw extending into the diaphyseal portion of the bone.

**Dr. Cooney:** Why is open treatment recommended for elbow fracture-dislocations? Can't the elbow be placed in extension, Dr. Braun?

**Dr. Donald Braun:** Closed treatment in extension would dislocate the elbow.

**Dr. Cooney:** Exactly. The elbow would be dislocated by placing it in extension to reduce the olecranon. You have to put it in flexion. You could treat this type of olecranon fracture conservatively, but with the elbow dislocation, this requires flexion, and as a result the olecranon fracture cannot be treated without open reduction and fixation.

**Dr. Morrison:** The radial head was excised, and olecranon fracture was treated by open reduction and tension band wire fixation (Figure 3 (C)).

**Dr. Morrison:** At follow-up approximately two and a half months after the operation, the range of motion was 15 to 100°, pronation 70°, and supination 80°.



Fig. 3(C) — Lateral view demonstrates the tension band wire fixation of intra-articular olecranon fracture. Radial head was excised.



**Dr. Miguel E. Cabanela:** When was motion started?

**Dr. Cooney:** The patient was hospitalized for two weeks, and motion was started at 10 days. The patient had a hinged elbow Orthoplast splint. In these situations, motion is begun between seven and 10 days. We do not wait three weeks. That is too long because of the possibility of anterior calcification. Myositis ossificans is much more severe if you wait longer than three weeks.

**Dr. Cabanela:** With this treatment, you can start motion in two to three days after the procedure, and the tension enhances the bony union. The longitudinal screws or pins should be extended down into the shaft of the ulna 4 or 5 cm below the fracture site. However, screws that are long enough to go that far down into the shaft usually are not very strong and may break. I have seen now two or three Leinbach screws that have broken.

**Dr. Cooney:** That is a good point. We tried to get cortical fixation with K-wires placed across the fracture.

#### Case 4

**Dr. Morrison:** A 23-year-old man suffered a

fracture of his cervical spine and injured his elbow in a motorcycle accident (Figure 4 (A) and (B)).



Fig. 4(C) — Lateral view of reduction shows that radial head is reduced but that bone fragment may be present within joint.

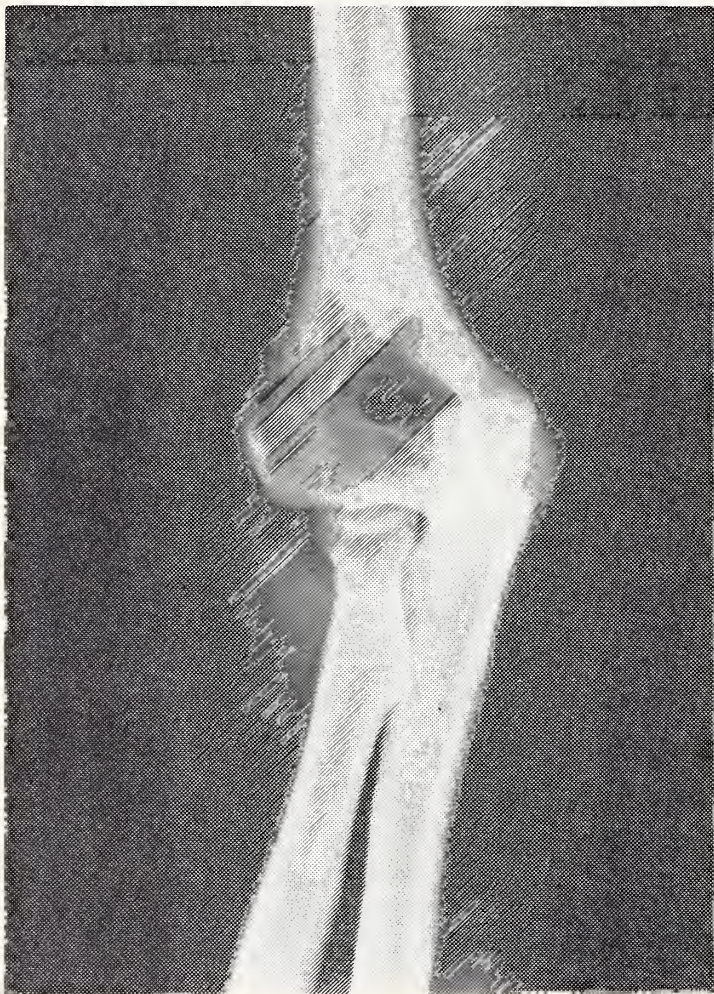


Fig. 4 (Case 4) — Dislocation of right elbow. (A-left) — Anteroposterior and (B-right) — lateral views of anterior dislocation. Lateral view shows small fragment within joint.



**Dr. Lee A. Christoferson, Jr.:** The patient has a medially dislocated olecranon and possibly a small bony fragment.

**Dr. Morrison:** What should be done?

**Dr. Christoferson:** After testing the neurovascular status, I would attempt to reduce the fracture in the emergency room.



Fig. 4 (D) — At four weeks, elbow has redislocated and heterotopic bone is noted on the lateral view. Open reduction from medial and lateral approaches was necessary to obtain reduction and remove fracture fragment from coracoid process which was present in the elbow joint.

**Dr. Morrison:** Reduction was done in the emergency room, and the arm was placed in a posterior plaster splint. The roentgenograms show that the fracture might be subluxed somewhat anteriorly, but it is not flexed past 90° (Figure 4 (C)). It was decided that the patient was to return in two weeks for removal of the splint and early elbow motion in an Orthoplast hinge splint with block to full extension. The patient did not come back until four weeks later; his splint and dressing were off, and he complained of pain in his elbow. The elbow was again dislocated (Figure 4 (D)). Will the dislocation be easy to reduce?

**Dr. Christoferson:** No. I doubt whether it can be reduced by closed methods.

**Dr. Morrison:** Closed reduction was attempted but was unsuccessful. Open reduction was necessary. The fracture was approached laterally and medially to release fibrous adhesions, remove intra-articular fragments, and obtain reduction. The medial epicondyle was osteotomized to expose the joint.

**Dr. Cooney:** Review of the original roentgenograms reveals that a coracoid fracture into the joint was missed. Open reduction revealed the coracoid process, and a number of intra-articular fragments in the joint were found to be blocking reduction. These fragments were removed. The fracture probably had not been reduced initially.

**Dr. Dobyns:** Roentgenograms can never determine stability as well as moving the elbow through its range of motion can.

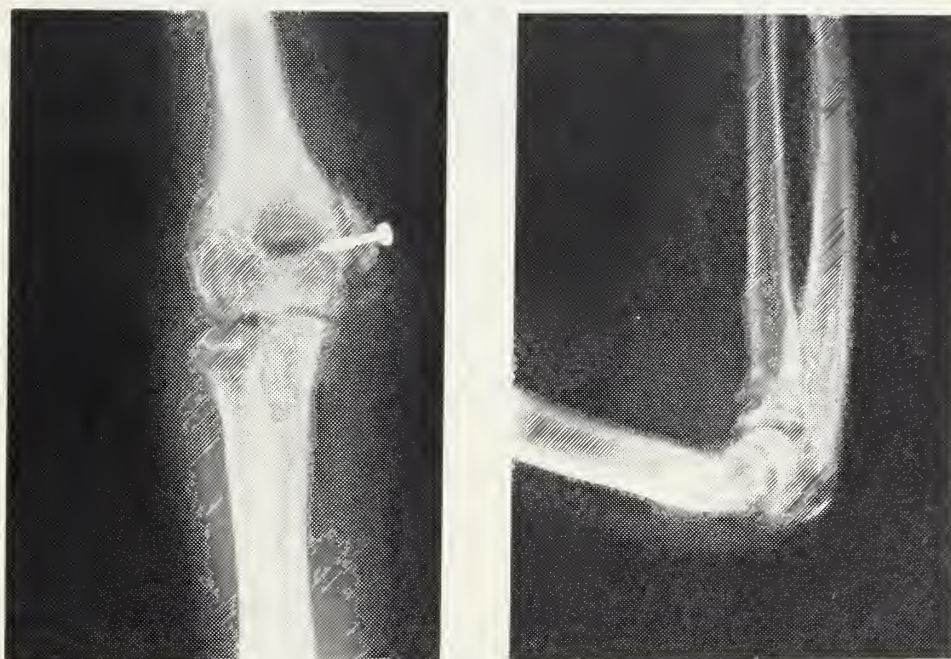


Fig. 4(E-left) and (F-right) — Roentgenograms at two months demonstrate that reduction has been maintained and that minimal heterotopic bone has formed. Elbow motion was satisfactory.



**Dr. Morrison:** At two months, the patient had 20 to 135° flexion, with a stable elbow joint and no pain (Figure 4 (E) and (F)). After open reduction, he was treated with early motion and a hinged Orthoplast elbow spint.

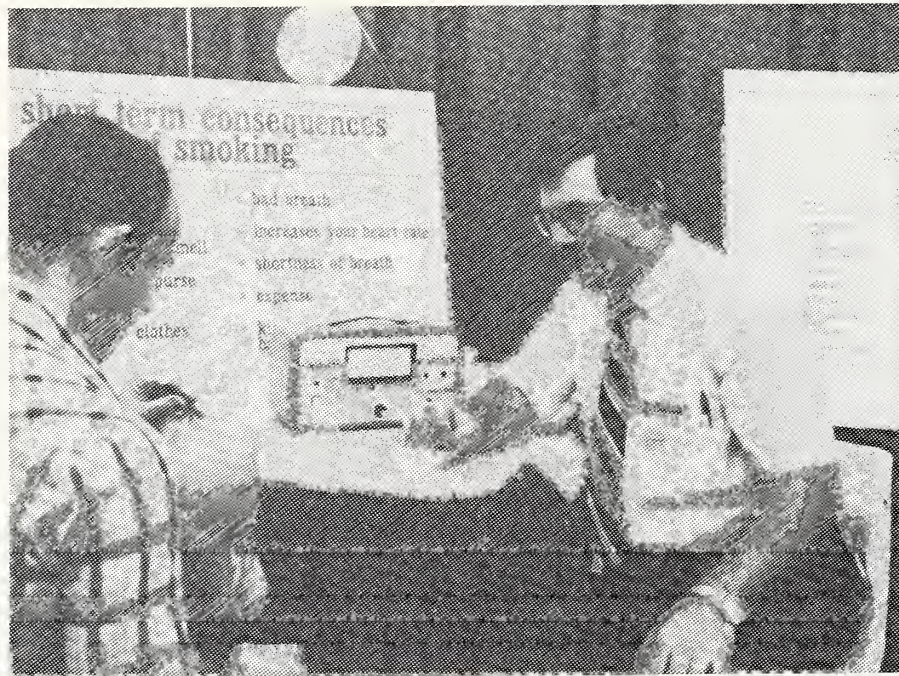
### Conclusion

**Dr. Cooney:** In the treatment of elbow fractures and dislocations, there are three points to remember: (1)

early motion of the elbow is generally better than delayed motion; motion should begin around one week or 10 days after the soft-tissue trauma has resolved; (2) the use of a hinged elbow splint of the Orthoplast type is helpful in maintaining the elbow motion and preventing subluxation and pistoning; and (3) a surgical approach to the elbow is necessary for intra-articular fractures to ensure anatomic alignment with early mobilization after secure internal fixation.

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MMA State Fair Exhibit

Dr. Sheldon Burns, Minneapolis, one of the 22 MMA physician volunteers, is administering a Carboximeter test. The MMA Public Health and Education Committee and the MMA Department of Communications annually plan and create an MMA exhibit at the Minnesota State Fair. The 1980 exhibit titled "Don't Smoke, Don't Choke, Don't Croak" was visited by over 15,000 Fair goers, and was co-sponsored by the Minnesota Department of Health. Photo by Roger Johnson



# Minnesota Medical Association

## Conversation with Dr. Robert W. Reif, State Representative



**Dr. Richard Reece:** Dr. Reif, you are the only physician in the Minnesota House of Representatives. When and how did you get interested in politics?

**Dr. Robert Reif:** It's a long story. I got interested years ago when the original Joint Senate/House Legislative Committee on Medical Education was formed. Hearings were held by the Committee to consider the shortage of physicians, rural family physicians in particular. Representative Fitzsimons, Representative from Northwestern Minnesota, was then Chairman of Appropriations in the House. He initiated these hearings, because his town was without a family doctor, and he was interested in improving the situation throughout the state.

I was involved, at the time as a physician in private practice and as a member of the Education Committee of the Minnesota Academy of Family Physicians, then the Academy of General Practice. Subsequently I became the state president of the Academy of Family Physicians and became involved in the legislative arena. I appeared and testified often.

In 1977, there was a move in the Legislature to declare medical records the property of the patient. The author was my own State Representative, a chiropractor. I was disappointed with the legislative process and fed up with other things, as were other citizens of Minnesota, so I decided to run in 1978.

**Dr. Reece:** Were you elected in 1978?

**Dr. Reif:** Yes, and sworn in in 1979. I replaced Maurice McCollar, a chiropractor.

**Dr. Reece:** What were the main issues in the campaign?

**Dr. Reif:** In general, the big issue was excessive taxation in Minnesota. This included business taxes, and of course, the income tax.

Inflation, the high cost of running the government, the spiraling bureaucracy, those were the other issues. The issue that I felt particularly strongly about was the Metropolitan Health Board. I raised that issue and found that there was sympathy among my constituents for doing something about the Council. But, over all, medical problems did not seem uppermost in people's minds.



**Dr. Reece:** How do you now manage to combine a political career and a medical career, and how much time do you spend at each?

**Dr. Reif:** Well, I'm fortunate on many counts. First, in my role as Director of Medical Education at St. John's Hospital in St. Paul, which is a community hospital, I have control over the time I spend there. I can make prearrangements, work at odd times, and plan without conflicting with other departments. I have latitude. Also, I have an understanding superior. The executive officer of the hospital is knowledgeable about politics. He knows what I'm doing. He knows it is important for me to be there.

**Dr. Reece:** Describe your work as a physician legislator.

**Dr. Reif:** Well, we start the 6th of January. In the off years, it is later. The interim session this last year started January 22nd.

I was appointed to three committees: Appropriations, Health and Welfare, and the Labor and Management Relations. These committees meet at varying times. The most difficult schedule to follow is the Appropriations Committee; that Committee meets every morning in the week that the Legislative Committees meet, Monday through Thursday. The pattern of legislative hearings are from Monday through Thursday every day. Friday is usually a day of no hearings until the end of the session.

The general sessions of the legislature are held in the afternoon, usually on Monday and Thursday. You see there is a state law that the Legislature, while it is in session, must meet at least every third day. So it meets Monday and again Thursday, and that way they can fulfill the letter of the law. So I start out my day with the Appropriations Committee, eight o'clock every morning, Monday through Thursday. After the hour of meetings, on Tuesday and Thursday I go into the Health, Welfare, and Corrections Subcommittee of Appropriations for another hour. On Tuesday and Thursday the Policy Committee on Health and Welfare meets from 10 to 12, and on Monday we have the Labor and Management Relations Committee from 12 to 1:45 p.m. Monday and Thursday afternoons the general session usually starts at two o'clock and can last a varying period of time.

I am fortunate, because our hospital is about four minutes from the capitol by freeway. So almost every noon I drive over to the hospital and catch up on my business of the day. I stay there until it is time to go back to the Capitol, eat my lunch either with staff there conducting business during the lunch period, or I may have lunch in my office and try to conduct business there. I then go back to the Capitol and follow the floor session. I make telephone calls or do whatever constituency business I have, then go back to the hospital.

**Dr. Reece:** What constituency do you serve?

**Dr. Reif:** I represent District 49B, which is, in general terms, White Bear Lake.

**Dr. Reece:** How many physicians are there in the House?

**Dr. Reif:** There are 134 members of the House of Representatives, and I am the only medical doctor.

**Dr. Reece:** Do you find your medical background is helpful?

**Dr. Reif:** It has been extremely helpful from a number of viewpoints. For one thing, colleagues seek medical advice, personal, family, or whatever, simply because of the convenience. I do the same thing when I seek information from lawyer colleagues. The chairman and members of the Health and Welfare Committee, or the Appropriations Committee will frequently ask for an opinion. This sometimes happens even up on the floor of the House during debate on a health bill.

**Dr. Reece:** Do you think we should have more doctors in the House?

**Dr. Reif:** Definitely. I'm lonely up there. I could use lots of help, of course. If you believe in a citizen legislature, as I do, then you must believe that there should be legislators from all walks of life, willing to serve, including doctors.



**Dr. Reece:** Have you learned anything from serving in the Legislature about the public's perception of medicine?

**Dr. Reif:** Among legislators, there is a general tenor, general feeling that medicine is not to be trusted.

**Dr. Reece:** Why not? Are we considered a monolithic monopoly?

**Dr. Reif:** The AMA is to some extent, but I don't hear the Minnesota Medical Association indicted as such. The AMA is regarded by some as a huge organization that is only interested in its own self-aggrandizement or its own self interest. The public be damned. Never mind what the medical costs are. Most legislators think organized medicine in general is only interested in feathering its own nest. When it comes to the individual physician, every legislator, I know, has an excellent relationship with his personal physician.

The public has less mistrust of organized medicine than before. This is particularly true in Minnesota. Legislators are much more interested in thinking about how we have it here, and how our physicians in this state are responding, organized or unorganized. But when it comes to the public at large, I find it hard to judge, because we hear mostly from self-interest groups such as welfare recipients, disabled, elderly people, the people who think of themselves as spokespeople, and they sometimes point an accusing finger at organized medicine. But, they are always quick to say, "Now, not all doctors are that way."

**Dr. Reece:** Do you think the Minnesota Medical Association, particularly the Socio-Economic Affairs Division, has impact on the Legislature?

**Dr. Reif:** Definitely, yes. I've been impressed on a number of scores, not just from my experience in the Legislature. I also am interested in the MMA's Socio-Economic Affairs Division's impact on the local regulatory agency, the Metropolitan Health Board, as I am a committed adversary of that agency. When I see the way our Association, the Physician's Metro Health Force, is able to gear up to put people on task forces, to monitor the task forces right from the start, to see the reaction when the guidelines come down, to see the way the Association can meet in special groups or task forces of their own, then I'm impressed.

**Dr. Reece:** Would you say the Association "steers" the legislature on HSA?

**Dr. Reif:** Oh, I wouldn't presume to say "steer," but at least they influence. I think you can honestly say the Association influences and influences tremendously. You have talented people working in the Division of Socio-Economic Affairs. The Division is organized in a manner that allows the Association to act rather than to just react. I'm impressed with the job the entire Association, its staff and lobbyists or legislative representatives, are doing.

**Dr. Reece:** As a physician with a scientific background, do you find the adversarial process frustrating? Have you adapted?

**Dr. Reif:** Once you've attended many hearings, and I did before I took this job, you appreciate the legislative process as a series of adversarial contests. That's what participative democracy is about. People engage one another in discussions which can become heated. But out of it has to come a viewpoint that either represents one side winning over another side, or at least a consensus where you can adjust and find some accommodation to both viewpoints. And that, it seems absolutely demands an adversary relationship. There's nothing wrong with that.

**Dr. Reece:** So you think heat sometimes generates light?

**Dr. Reif:** Only in the fire is steel formed hard and firm.

**Dr. Reece:** For a fiery statement, that is a well-tempered remark. How do you like serving on the Health and Welfare Committee?



**Dr. Reif:** I think you're talking about the Policy Committee. I find that much more policy, more effective policy, is probably formed by the Appropriations Committee, the Health Division of Appropriations. A bill that requires money has to go through Appropriations. I find it interesting being on Appropriations, an invaluable experience, just invaluable.

**Dr. Reece:** Could you give us some concrete examples of the kind of issues that arise there?

**Dr. Reif:** I'll give you an example. Are you familiar with pre-screening? Pre-screening means that everyone the year or two before qualifying under Medicaid/Medicare will be screened by a team, consisting of a public health nurse and social worker. That screening team will write a prescription for that person; literally prescribe what kind of care that person will need and whether or not it has to be done in an institution.

It's no secret, I'm sure, to you or to anybody else — it shouldn't be — that 70 percent of the Welfare budget goes to pay for people in nursing homes. So pre-screening is the big idea in monetary terms. Many clear-thinking socially-minded people believe we can save money by pre-screening, so they've described these functions in a pre-screening bill that was heard before the Policy Committee. We had a lot of argument about it, but nothing happened because it required that there will be an appropriation. So, when it finally came down, it had to be heard before the Appropriations Committee, before the Health Division of Appropriations. That is the point at which the whole question of whether or not we were going to have pre-screening was decided before that Appropriations Subcommittee. No matter what goes on over in the Policy Committee, the real test of the matter is in Appropriations — if the money is going to flow to make it happen.

**Dr. Reece:** I, for one, was not aware that 70 percent of the Welfare budget for Medical Assistance went to nursing homes.

**Dr. Reif:** Approximately.

**Dr. Reece:** And you're saying the pre-screening committee would serve as a gateway for entry into the nursing homes?

**Dr. Reif:** Yes, the main aim is to keep people out of the nursing homes. To do that, this team would determine what kind of care the patient would need. Let's say, for instance, that you've developed thrombophlebitis and you're sixty-four years old and you've got huge varicose ulcers. If something doesn't happen to make things better, you're going to have to go into the nursing home because you can't take care of your ulcers at home. But the pre-screening team comes out, or the screening team, comes out to your home and decides you can be treated at home if you can get some home health aides. Because of the aides, you won't have to get up and walk around your house, and do all these things that keep you on your feet. Instead of sending you to a nursing home, we're going to keep you at home, but you're going to have a home health aide here to help you do your chores around the house. We'll send a nurse in to dress your leg.

Now we were able to insert, through the working of our lobbyists for the Minnesota Medical Association, a clause that said the local or personal physician may be involved in that process, if he or she wishes or if the patient requests it. But it is not absolutely necessary that the physician will be involved. In other words, there are screenings that can go on without the physician involved. This is the type of issue we contend with that requires confrontation and compromise.

**Dr. Reece:** Let's talk about two other major issues.

One is the HMO movement, which is more powerful in Minnesota than in any other state, and two, the health planning movement. Just very briefly, in broad terms, what do you perceive will evolve for each in the next ten years?

**Dr. Reif:** Well, you may know the final bill to be considered before the Legislature this year was the so-called de-regulation of HMOs. As you probably know, HMOs now must, by law, provide certain basic services. In keeping with the whole spirit of competition and the enhancement of the open market theory to drive health care costs down, there was a bill proposed to deregulate HMOs. HMOs, in other words, could offer anything in the line of services as long as they were open about advertising about it. Then individuals could seek the kind of HMOs that they wanted.



For example, if I did not believe in abortions, I could go find an HMO that did not pay for abortions. It could be a little cheaper. Or, if my wife and I decided we're not going to have children, I could go to an HMO that didn't provide OB services, and that would be a little cheaper. So the whole concept was to let HMOs operate just the way every other kind of business operates. Let it be open market, and advertising those things, openly that are offered. Let the patient, let the client, let the purchaser, decide what he or she wants.

That bill did not have many hearings, and due to clever manipulations by the Senate majority leader, it almost passed. It passed the Senate, but it was rejected by the House Conference Committee. It was wrapped up in a so-called garbage bill that had four or five other important issues attached to it, and the whole idea then was tossed out.

**Dr. Reece:** But that same HMO bill will arise again.

**Dr. Reif:** Yes it will arise again. If you look at what our so-called "think tanks", the people who are in the think tanks now in the whole area of health care delivery, I'm talking about the McClures, the Ellwoods and Durenbergers . . . are talking about open market competition. They're saying: let's go back to free enterprise to drive the health care costs down. Regulation hasn't done it; why don't we try this? And there's a body of experts who agree with them.

**Dr. Reece:** Yes, Durenberger's bill, was based largely on ideas of Ellwood and by Enthoven, out at Stanford. It is a consumer choice health plan, and that would allow various gradations and types of HMOs.

**Dr. Reif:** Exactly. I see a general effort to open up the whole field of health care delivery in a more open fashion, a more competitive fashion. On the other hand, we've got many liberals who believe the government should protect, provide, and furnish just about everything for the public. And we have those people who are very much concerned about the so-called police function, to protect the public by government. They feel the disadvantaged will be abandoned if we open it up to utilization of open market and competition.

**Dr. Reece:** I was just noticing on the television today that the SHARE plan is making a big push to cover Medicare patients with an HMO. This HMO is an illustration about what you're talking?

**Dr. Reif:** Yes, McClure spoke to a joint meeting, a joint conference meeting of the Senate and House last year, and he spoke very strongly about the need to look at Medicare/Medicaid, which is costing us so much money. The SHARE concept is a tailor made HMO concept that would apply for Medicare/Medicaid patients.

**Dr. Reece:** What do you think of this pluralistic, interlocking HMO approach, a system of compulsory consumer choice health plans?

**Dr. Reif:** Well . . . I think it has potential. There are many of my associates who have entered into not one, but several membership rosters on HMOs and deliver prepaid health care to a number of different groups through a number of different plans. HMOs are certainly opening up the health delivery field. It's putting to test the theories, if nothing else. And I see nothing wrong with that. You know, I think any physician, if he's worth his salt should be willing to compete on any of those grounds to give better care to his patients.

**Dr. Reece:** Will the current physician excess escalate this competitive HMO process?

**Dr. Reif:** I prefer the term "physician mal-distribution." I know many communities that would go to war with you when you talk about physician excess. They're striving hard to attract physicians, and they won't come. We have a mal-distribution in both specialty groups and in geographic locations.

**Dr. Reece:** Now the government economists' theory is that too many will produce a spillover effect. In other words, if you increase the number of physicians and create an excess, they will spill over into the rural areas. Do you believe that's going to happen?

**Dr. Reif:** To some extent, in some of the specialties, but I'd be hard pressed to find out how a neurosurgeon



could go into a town of 800 and practice medicine. You know, by his specialty, by the kind of person I think he is, by his personality, that he'd probably never do it. Secondly, if he would, he'd be ill prepared to do it and would be unable to practice the kind of medicine they're looking for in that community. In a sense, he would have wasted all of his professional training.

**Dr. Reece:** I agree. Well-educated specialists, whether they be architects, lawyers, or professors, have to congregate in urban areas to practice what they've been trained for. Why, even health planners cluster in the cities.

**Dr. Reif:** I see "spill-over" happening in family practice, in internal medicine and to some degree in pediatrics. Five years ago, smaller communities were unable to attract men in the specialty areas of internal medicine and pediatrics. That has changed.

**Dr. Reece:** Would you agree that Minnesota has done an excellent job through family practice programs in training physicians for rural practices?

**Dr. Reif:** We've gone a long way, farther than anyone else. But it's still a great disappointment to me to see the lack of interest, by our training centers, in providing the physicians the communities seek. Look at the resources that we're piling into training of medical specialists and sub-specialists. Then look at the distribution of physicians. It seems to me medical schools, our great educational centers, and our professional associations could better plan the number of specialists, the number of generalists, and where both might practice.

**Dr. Reece:** You don't think marketing forces take care of that?

**Dr. Reif:** Well, if we wait for marketing forces, what will happen is we'll have a lot of people trained unnecessarily. You could say the same thing about teachers, and I really inveigh against centers that trained our elementary and secondary school teachers for many years and turned out a disgruntled, frustrated group of people who were trained professionally but who found no place for employment. I think that's a poor way to go.

**Dr. Reece:** So you're saying the specialty societies and the medical centers are still looking inward rather than systematically looking at the requirements of the public.

**Dr. Reif:** I believe so.

**Dr. Reece:** What do you think is going to happen in the next ten years? Do you think that these competitive forces, which are strong already in Minnesota are going to become increasingly powerful? Do you see a subsidence of the regulatory sector?

**Dr. Reif:** You're speaking in the health care delivery area.

No, I don't see a subsidence of the attempt to regulate. There will always be entrenched bureaucrats. There's still a strong inclination to regulate and for all kinds of reasons. But I suspect the attempt to deregulate is gaining strength. I think we're going to swing away from regulation.

**Dr. Reece:** Do you think that MINNPAC (the Minnesota Medical/Political Action Committee) has any effectiveness influencing the legislative races?

**Dr. Reif:** I think MINNPAC is effective. I've benefitted from it, so my answer has bias, but when I try to recruit my colleagues to join MINNPAC, I hear over and over again, "I want to put my money where I think it's going to do the most good," or "I want control over my funds, so that I can tell where they are going to go." My response is that for the biggest bang for the buck, you have to put those funds together, so that you can select people in a unified way and support people. A single person simply doesn't have the resources to be able to make that impact. Not only monetary resources, but the investigatory resources to look into all the races and to say, "these are the people who have a chance to make a difference." We organize that way in every other form of our existence, you know.



**Dr. Reece:** It's expensive to launch a legislative campaign, isn't it? How much is it? In time, as well as money?

**Dr. Reif:** Well, I can speak personally right at the moment, because I'm involved in a reelection campaign. I just happen to have a sample of my brochure. Printing is extremely expensive. So is mailing. It costs almost ten cents a piece to mail. Most of our House Districts have about 30,000 residents, or 7,500 to 10,000 households. If you're going to mail a brochure, it's quite costly. Add to that expense of advertising in the newspapers, or in the rural area, the radio. There are other expenditures that maybe don't show up — the signs that you have to print up, and then the expenditure of time.

I'm so impressed when I see the people who volunteer to serve on our campaign committees. It's somewhat similar to the way physicians volunteer to serve in our professional associations or in our hospitals on the various committees — a tremendous amount of time is involved. In my last campaign, we spent \$18,000. Now the special campaigns for the House have gone as high as \$25,000 and the time expenditure is six weeks.

**Dr. Reece:** I might as well ask, what party are you?

**Dr. Reif:** I'm an Independent-Republican.

**Dr. Reece:** We are now in a presidential year. This interview would be incomplete without my asking you how do you think the relative powers of the Independent Republicans and Democrats are in Minnesota this year. Are you in a predicting mood?

**Dr. Reif:** I try not to be. The Republicans do have a reasonably good chance. If we weren't dealing with the advantage of an incumbent President, I'd say that the chances are excellent, perhaps even better than even. If we look at what the polls are saying, that would tend to bear it out. However, not for one minute can we take for granted it will stay that way. The President is a shrewd politician; he has tremendous ability to recover and to exploit the advantages of his office. And I believe it will be an extremely close race right down to the wire. Given the uncertainty of the international situation, you'd have to say that it's an open bet either way.

**Dr. Reece:** Too close and too early to call?

**Dr. Reif:** Yes, but let me just add one thing . . . when you talk about party, you tend to forget about, at least you don't stress, and I think it's most important, in Minnesota that you should truly talk about conservative vs. so-called liberal, because that concept crosses party lines. And if I were to look at the really important issues that come before us, they are decided much more likely along those lines than they are across the traditional party line. We see a lot of joining of forces of members of both parties in conservative issues vs. the liberal issues. And we now have a predominance of conservative legislators, rural and urban.

**Dr. Reece:** Be they DFL or Independent Republicans.

**Dr. Reif:** Right, I can show you all kinds of instances where the conservative block really held sway, rather than the parties.

**Dr. Reece:** Do you think Gov. Quie appreciates that?

**Dr. Reif:** Oh, yes, he's an astute politician. The majority leader of the Senate aptly described him as a masterful politician, and the beauty of it — he comes across without any of the derogatory implications of that term. He's a down to earth, common man, but very astute in his field of politics.

**Dr. Reece:** Would you classify him as understated and effective?

**Dr. Reif:** I think you could use both those terms.



**Dr. Reece:** One last comment . . . being such a busy man how does your family tolerate this dual life of yours? How many children do you have?

**Dr. Reif:** I have six children. My family has been quite understanding. You know, I was in private practice for 20 years, a good share of that by myself, solo practice. And I think they recognize that there are times when duty calls in many other spheres.

**Dr. Reece:** Are you a native Minnesotan?

**Dr. Reif:** I was born and reared in what is now called a ghetto area of St. Paul, Thomas-Dale, commonly called Frog-Town.

**Dr. Reece:** You were educated in Minnesota?

**Dr. Reif:** Educated in Minnesota, right.

**Dr. Reece:** Went to Medical school here.

**Dr. Reif:** University of Minnesota.

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# Minnesota Medical Association

from

## Division of Socio-Economic Affairs

James H. Sova, Assistant Executive Vice President  
Lynn R. Gruber, Director, Department of Medical Services and Research  
George C. Lohmer, Jr., Director, Department of Health Planning  
Charles W. Wiger, Director, Department of Legislative Affairs

### Department of Legislative Affairs

#### *Groundwork Being Laid for 1981 Session*

The Department of Legislative Affairs is actively meeting with legislative candidates to inform them of MMA's 1981 legislative priorities. These priorities include as follows:

- Eliminating unnecessary and duplicative provisions of the Preschool Screening Law.
- Opposing mandatory chiropractic and optometric services in HMOs.
- Opposing legislation that allows optometrists to use drugs for diagnosis and treatment of eye problems.
- Requiring motorcyclists to wear helmets.
- Supporting a statutory definition for brain death.
- Requiring all tablets and capsules of prescription drugs dispensed in Minnesota to carry an identifying mark (see next section for further information).

Physicians and auxiliaries are taking this opportunity to arrange meetings with their local legislators. In addition to discussing the above items, it is also important to emphasize the MMA's general opposition to governmental intervention in professional and private life. Your MMA Committee on Legislation strongly encourages you to share these concerns with



#### **Your MMA Committee on Legislation**

1st row (left to right): G. R. Diessner, M.D., (Rochester), Merle S. Mark, M.D., Chairman, (Minneapolis), Duane Orn, M.D., (Minneapolis), Kathleen A. Meyerle, Dept. of Legislation, (St. Paul), Charles W. Wiger, Dept. of Legislation, (St. Paul), 2nd row (left to right): Roy H. Good, M.D., (Faribault), Lee Beecher, M.D., (St. Louis Park), Chester Anderson, M.D., (Hector), Wallace E. Mathews, M.D., (Mankato), Thomas Stolee, M.D., (Duluth), Dorothy Diessner, guest, Auxiliary Legislative Co-Chair, (Afton), Vernon Sommerdorf, M.D., (St. Paul), Gayle Whitesell, guest, Auxiliary Legislative Co-Chair, (Buffalo), L. Ashley Whitesell, M.D., guest, MINNPAC Chairman, (Buffalo)

NOT PICTURED: T. L. Fritsche, M.D., (Marshall), Edwin F. Luh, M.D., (Fergus Falls), Robert A. Scott, M.D., (Minneapolis)



your area legislative candidates. For more information on any of these issues, please call the Department of Legislative Affairs (612) 378-1875.

*New MMA Proposal Requires Drug Identification*

Pursuant to action by the Board, the MMA will be proposing legislation in 1981 to require all tablets and capsules of prescription drugs dispensed in Minnesota to carry an identifying mark. At virtually no cost to the manufacturer or drug purchaser, the proposal would be of a great deal of help in poison identification and treatment and eliminate consumer confusion between various drug products.

A crucial step in treating an emergency poisoning victim is the identification of the contents of the product ingested or exposed to. The faster identification is made, the earlier appropriate treatment can begin. Systems such as POISINDEX<sup>®</sup> are available to identify tablets and capsules by imprint monogram. If no mark is on the drug, determination of the suspected poison then requires laboratory analysis of blood, urine, gastric contents or other fluids or tissues. Valuable treatment time is lost in this process.

The proposal is simply an extension of the policy in the 1975 Drug Product Selection Law that the consumer has a right to know what drug they receive and who manufactures that drug. The law requires manufacturers to label the drug container and the pharmacist to put the name of the drug and manufacturer on the prescription label. With the increase in the number of generic drugs manufactured to look like the brand name product, it is a logical step in the law to require tablets or capsules to be individually identified to avoid confusion.

For companies not now marking drugs, there will be some initial costs in equipment acquisition. Cost estimates to imprint drug products range from 2 cents to 7 cents per 100 doses depending on the form of the drug (eg: capsule, tablet, coated tablets, etc.); however, with the current available sources of drugs with identifying marks and the competition in the drug market, there should be no adverse impact on costs to the consumer or the availability of drug products.

Several states have passed similar legislation and the federal government is considering requiring a National Drug Code marking system. The concept of drug identification is supported by the American Association of Poison Control Centers and the American Pharmaceutical Association. The American Medical Association adopted a resolution at its 1980 Annual Meeting supporting action, either by the states, federal government or pharmaceutical manufacturers, to imprint solid drug forms.

**Department of Medical Services and Research**

According to reports from the Minnesota Departments of Revenue and Finance, the State of Minnesota is facing a \$90 million deficit next June 30. Due to the provision in the Minnesota Constitution which prohibits the State from operating with a deficit, Governor Quie has asked all his department heads to make recommendations on possible ways to cut their budgets. The Minnesota Department of Public Welfare (DPW) is one of the departments in which major deficits are projected through June, 1981. The Medical Assistance Program (MA), administered by DPW, is a program in which many Minnesota physicians are involved.

While Governor Quie has exempted direct payment to Medical Assistance recipients from the imminent budget cuts, other areas of the MA Program are being scrutinized as possible items to cut. Three options under consideration are to: (1) review reimbursement levels from MA providers and deduct a percentage from the remittance; (2) review the optional services now being provided to Medical Assistance recipients such as, dental services, pharmacy services, and transportation services; (3) make the eligibility standards for Medical Assistance more strict. The Minnesota Legislature would have to make definitive decisions on the second option.

To date, officials of the MA Program have been able to trim \$77,000 in administrative



## DIVISION OF SOCIO-ECONOMIC AFFAIRS

costs and overhead, however, due to this adjustment, physicians who are providers for the MA Program may experience a slowdown in claims being processed, and a slowdown by DPW in answering telephone calls. In addition, fewer audits of MA providers will occur due to a cut in travel expenses for DPW staff.

Through MMA staff liaison to the Department of Public Welfare, involvement by members of the Committee on Medical Service with DPW officials, and through periodic meetings between MA officers and DPW Commissioner Arthur Noot, the members of the Minnesota Medical Association have a voice in impacting policies which may affect them through actions taken by the Minnesota Department of Public Welfare and during the coming weeks will be relating the latest developments concerning the budget cuts in DPW programs to all MMA members.

### Department of Health Planning

#### *Hearings on Appropriateness Review Scheduled Statewide*

Between now and the end of November, Health Systems Agencies throughout the state will be scheduling hearings to discuss their first cycle of Appropriateness Review findings for the following institutional health services: End-Stage Renal Disease, Open Heart Surgery, Cardiac Catheterization, and Megavoltage Radiation Therapy.

Unlike Certificate of Need (CON) Reviews which review the need for *new* institutional health services, the Appropriateness Review (AR) process is established to review *existing* services and facilities. Health Systems Agencies, in their study of the "appropriateness" of services in their geographic area must consider the community need for each service; how available, accessible, cost-effective and financially viable the service is; and its quality. The HSA may suggest improvements in a service, or "remedial actions" if the service is found "inappropriate". There are no direct statutory or regulatory sanctions to enforce these remedial actions, although indirect sanctions could be applied through such mechanisms as CON, rate review, and third-party sanctions.

As required by the new health planning legislation (P.L. 96-79), Appropriateness Review findings of the Health Systems Agencies will be forwarded to the State Health Planning and Development Agency for statewide review as well. The SHPDA and HSAs in Minnesota have established a uniform schedule for review of all institutional health services. There are five review cycles, with the final one scheduled for completion in May, 1983.

For information on the hearing scheduled in your area, contact your local Health Systems Agency staff or the Minnesota Medical Association Department of Health Planning, (612) 378-1875.

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## MINNPAC

### *MINNPAC Board Busy Assessing Races and Contributing to Candidates*

Who does medicine support in the important legislative and congressional races? Find out in the upcoming "Physician-Auxiliary Election Preview" which will be distributed to the medical community in October.

The MINNPAC (Minnesota Medical Political Action Committee) Board has been meeting with various candidates and nearly \$60,000 has been or will be contributed to worthy campaigns. An upcoming "Election Preview" will indicate those legislative candidates receiving MINNPAC support, and in addition, the congressional candidates supported by AMPAC will be indicated.

Many of the projected general election winners can already be determined since several candidates are not opposed and others faced their strongest opposition in the September 9th primary. The following candidates have no opposition in the general election:

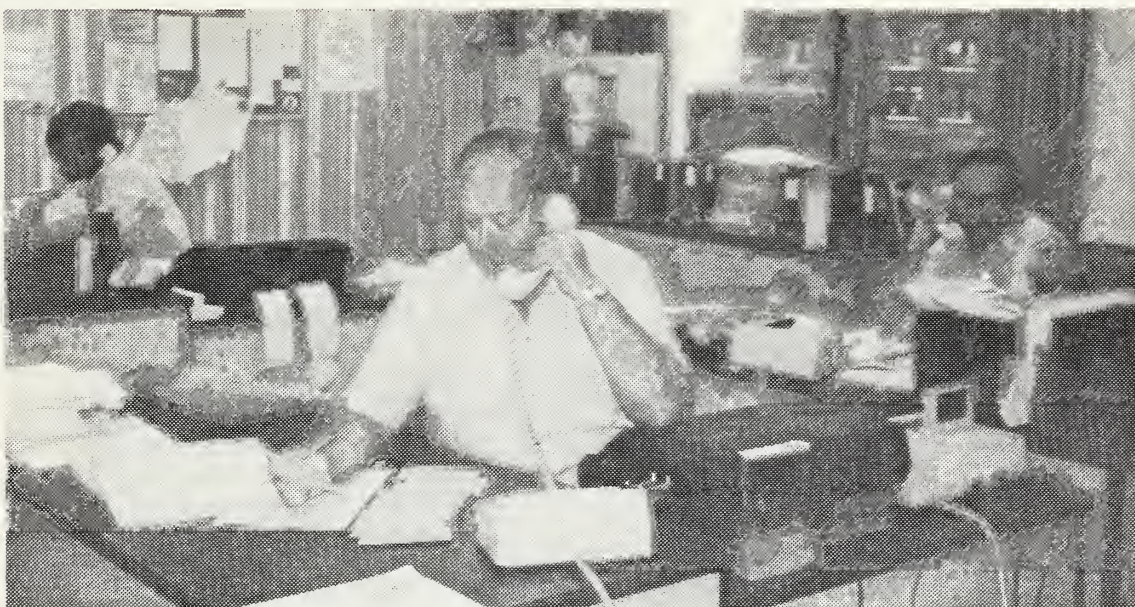
### *Legislative Candidates with No Opponent in General Election*

#### Minnesota Senate (6 DFLers unopposed out of 67 races)

Senator Bob Lessard (DFL-International Falls, District 3), Ron Dicklich (DFL-Hibbing, District 5), Senator Doug Johnson (DFL-Cook, District 6), Senator Sam Solon (DFL-Duluth, District 7), Senator Hubert "Skip" Humphrey III (DFL-New Hope, District 44) and Senator Anne Stokowski (DFL-Minneapolis, District 55)

#### Minnesota House (12 IRs and 11 DFLers unopposed out of 134 races)

Rep. Dominic Elioff (DFL-Virginia, District 5A), Rep. Lona Minne (DFL-Hibbing, District 5B), Rep. Joe Begich (DFL-Eveleth, District 6A), Ben Gustafson (DFL-Duluth, District 7B), Rep. Steve Wenzel (DFL-Little Falls, District 12B), Rep. Adolph Kvam (IR-Litchfield, District 22A), Rep. Dave Jennings (IR-Truman, District 27B), Rep. Gil Esau (IR-Mountain Lake, District 28A), Rep. Henry Kalis (DFL-Walters, District 30A), Rep. Leo Reding (DFL-Austin, District 31B), Rep. Dick Kaley (IR-Rochester, District 33A), Rep. Elton Redalen (IR-Fountain, District 35A), Rep. Shirley Hokanson (DFL-Richfield, District 37A), Rep. Mary Forsythe (IR-Edina, District 39A), John Himle (IR-Bloomington, District 39B), Rep. Doug



William M. Chandler, M.D., (center) MINNPAC Director and member of the Minnesota Radiological Society is telephoning a colleague to join MINNPAC. Pictured with him are Quentin N. Anderson, M.D. (right) and Ronald E. DeCesare, M.D. (left). All are from Minneapolis.



## MINNPAC

Minnesota House (12 IRs and 11 DFLers unopposed out of 134 races) (Continued)

Ewald (IR-Minnetonka, District 40A), Rep. Jerry Knickerbocker (IR-Hopkins, District 40B), Rep. Sally Olsen (IR-St. Louis Park, District 41A), Rep. Robert Searles (IR-Wayzata, District 42B), Rep. Lon Heinitz (IR-Plymouth, District 43A), Rep. Gordon Voss (DFL-Blaine, District 47B), Randy Staten (DFL-Minneapolis, District 56A), and Rep. Ken Nelson (DFL-Minneapolis, District 59B)

In several other races, the incumbent doesn't face a strong challenge in the general election.

### *1980 MINNPAC Membership Total Approaching Record High*

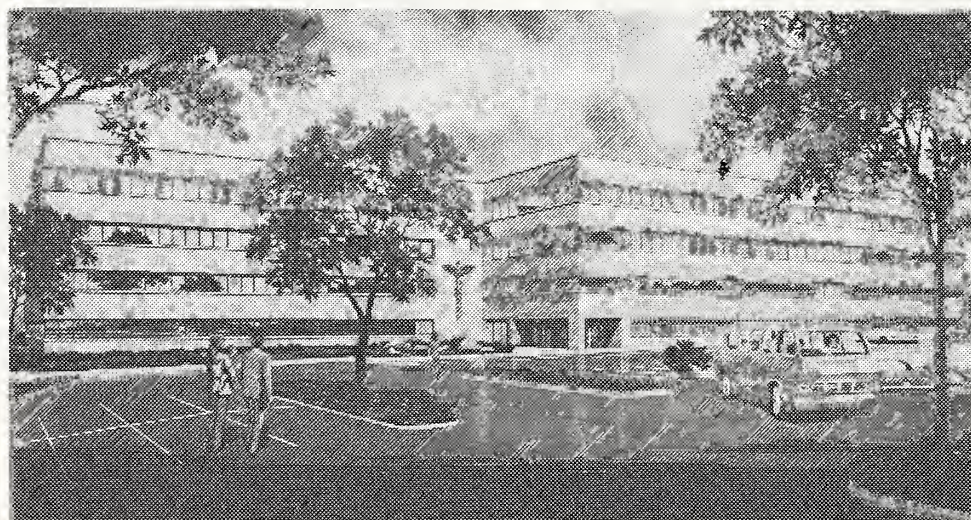
To bolster medicine's political effectiveness, MINNPAC has been actively working to recruit new members. Political action presentations have been made before several local clinics, hospitals and county medical societies. The response has been very encouraging and 1980 membership is now within striking distance of the record total of 1,140 members in 1978.

One new feature of the membership campaign has been for various specialty societies to participate in a telephone solicitation. Volunteers from the Minnesota Academy of Family Physicians, Minnesota Association of Ophthalmology, the Minnesota Psychiatric Society and the Minnesota Radiological Society telephoned their colleagues and urged them to join MINNPAC. The response was excellent. Pictured on the previous page are three of twelve volunteers from the Minnesota Radiological Society. The MINNPAC Board extends its deep appreciation for the enthusiastic efforts of the volunteers and to those of you who have become members.

### **We Are Moving!**

The Minnesota Medical Association and MINNESOTA MEDICINE will be moving into the new Health Association Center on October 9th. The address will be:

Minnesota Medical Association  
2221 University Avenue S.E., Suite 400  
Minneapolis, MN 55414  
Telephone: 612-378-1875





# Minnesota Medical Association

## CME in Minnesota

*An ongoing calendar of scheduled CME programs as well as important holidays, state and national medical meetings and other important dates extending into the future will be maintained in the MMA office. CME planners are encouraged to contact the office when planning future programs so as to avoid scheduling conflicts.*

Information for each entry below is arranged as follows: Name of program; Primary sponsor; Location; Date; Contact person.

Stuart V. Thorson, M.D., Chairman  
Subcommittee on CME Resources

### October, 1980

**Internal Medicine Review;** U of M Medical School; U of M Mpls.; Oct. 1-3; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Enhancing Your Financial Skills;** MMA, Hennepin County Medical Society, Ramsey County Medical Society; Decathlon Club, Mpls.; Oct. 9; CONTACT Dave Luth, MMA, Suite 900 American National Bank Bldg., St. Paul, MN 55101, 612/222-6366. (Management seminars will also be held on Oct. 7, 8, & 10 for medical office personnel.)

**Third Annual CNS Disease Symposium;** U of M Medical School with Hennepin County Medical Ctr.; Hennepin Co. Medical Ctr., Mpls.; Oct. 10; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Pediatric Seminar;** Minneapolis Children's Health Center and St. Paul Children's Hospital; Mpls. Children's Health Ctr., Mpls.; Oct. 10; CONTACT Daniel P. Kohen, M.D., 2525 Chicago Ave. So., Mpls., MN 55404, 612/874-6238.

**Joint Meeting, MN Society of Internal Medicine & MN Chapter, American College of Physicians;** St. Paul-Ramsey Med. Ctr.; Oct. 11; CONTACT Brian Campion, M.D., St. Paul-Ramsey Med. Ctr., 640 Jackson St., St. Paul, MN 55101, 612/221-3456 and Joseph Cardamone, M.D., Mercy Medical Center, 4050 Coon Rapids Blvd., Coon Rapids, MN 55433, 612/427-2200 Ext. 2367.

**4th Annual Current Concepts in Ophthalmology;** Mount Sinai Hospital; L'hotel de France, Mpls.; Oct. 11; CONTACT Mrs. Evelyn Peterson, Medical Staff Secretary, Mount Sinai Hospital, 2215 Park Ave., Mpls., MN 55404, 612/871-3700, ext. 1117.

**Neonatology;** Central Mesabi Medical Center; CMMC; Oct. 13; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.

**Annual Ob/Gyn Autumn Seminar;** U of M Medical School; Mayo Memorial Auditorium, Mpls.; Oct. 15-17; CONTACT CME Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Basic Cardiac Life Support;** North Memorial Medical Center, Mpls.; October 15-16; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Electrical Pacing in Diagnosis and Treatment of Cardiac Arrhythmias;** U of M Medical School; U of M Mpls.; Oct. 16-17; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Basic Cardiac Life Support Instructor Course;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Oct. 20-21; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Cardiovascular Disease Conference with Clinical Preceptorship;** U of M Medical School; St. Paul Ramsey Medical Center; Oct. 23-25; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Seminar for Directors of Medical Education;** MMA; Spring Hill Center, Wayzata; Oct. 24-26; CONTACT Teresa L. Rogstad, Suite 900 American National Bank Bldg., St. Paul, MN 55101, 612/222-6366.

**Poisoning: A Brief Symposium;** U of M Medical School; St. Paul Ramsey Medical Center; Oct. 24; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**ENT for Primary Care Physicians;** Mayo Foundation; Mayo Clinic, Rochester; Oct. 26; CONTACT Postgraduate Courses, Rm. 720, Plummer Bldg., Mayo Clinic, Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Clinical Reviews;** Mayo Foundation; Mayo Clinic, Rochester; Oct. 27-29; Nov. 10-12; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Principles of Colon & Rectal Surgery;** U of M Medical School; U of M Mpls.; Oct. 29-Nov. 1; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### November, 1980

**Fall Scientific Program; MN Society of Anesthesiologists;** L'hotel de France, Mpls.; Nov. 1; CONTACT David Byer, M.D., 2001 1st St. S.W., Rochester, MN 55901, 507/286-8701.

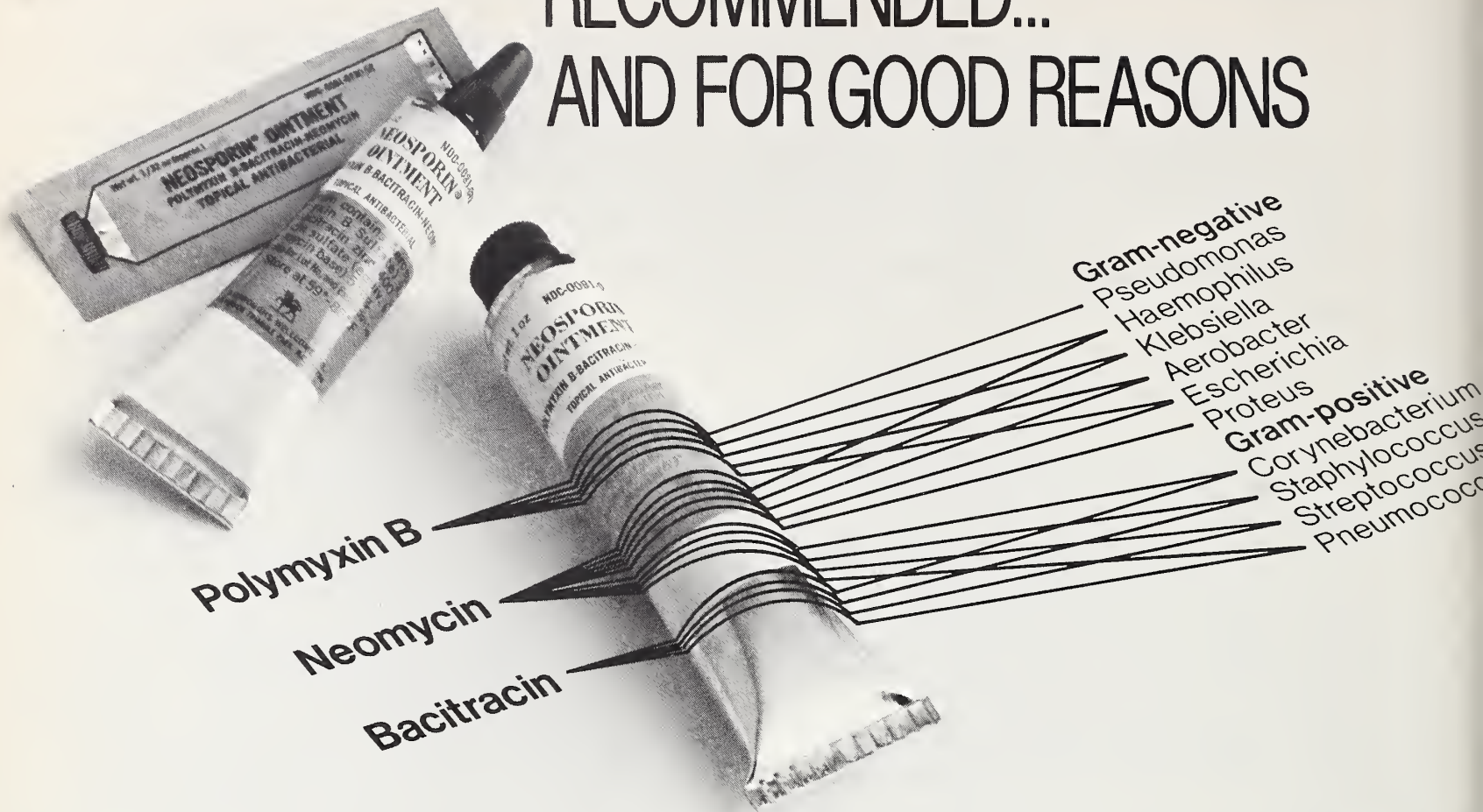
**Workshop on Heart Attack Prevention;** U of M Medical School; Spring Hill Center, Wayzata; Nov. 4-6; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Neonatal Resuscitation;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 6; CONTACT Mark Bixby, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Current Topics in Pulmonary Pathology;** U of M Medical School; U of M Mpls.; Nov. 6-7; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.



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**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations,

prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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## CME IN MINNESOTA

### November (Continued)

**Update in Oncology for Primary Care Physicians;** American Cancer Society, MN Div. Inc.; Radisson Hotel, St. Paul; Nov. 7; CONTACT Caryl Range, 2750 Park Ave., Mpls., MN 55407, 612/871-2111.

**Advanced Cardiac Life Support Course;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 7-8; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Update in Cardiology;** Mayo Foundation; Mayo Clinic, Rochester; Nov. 9; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Clinical Reviews;** Mayo Foundation; Mayo Clinic, Rochester; November 10-12; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Basic Cardiac Life Support;** November 12-13; see Oct. 15-16 entry.

**Ophthalmology for Primary Care;** U of M Medical School; Sheraton Ritz Hotel, Mpls.; Nov. 14-15; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Practical Therapy of Malignant Disease;** Duluth Clinic LTD.; St. Mary's Hospital, Duluth; Nov. 15; CONTACT J. G. Brueggemann, M.D., Dir. of Medical Education, Duluth Clinic, LTD., 400 E. 3rd St., Duluth, MN 55805, 218/722-8364.

**Endocrinology;** Central Mesabi Medical Center; CMMC; Nov. 19; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.

**Nordic Sports: A Scientific Approach;** U of M Medical School; Mt. Telemark, WI; Nov. 20-23; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### December, 1980

**Thirteenth OB-GYN Symposium;** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Dec. 5; CONTACT Milton Baker, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Winter Meeting, MN Obstetrical & Gynecological Society;** North Memorial Medical Center, Mpls.; Dec. 6; CONTACT Richard Bendel, M.D., Hennepin County Medical Center, 701 Park Ave. S., Mpls., 55415, 612/347-2750.

**Basic Cardiac Life Support;** December 10-11; see Oct. 15-16 entry.

**New Concepts of Otological Surgery and Clinical Problems in Otitis Media;** U of M Medical School with Lions International Hearing Center-Mpls., Chilean Medical Association, Chilean Society of Otolaryngology; Carrera Hotel, Santiago, Chile; Dec. 11-13, CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Oncology;** Central Mesabi Medical Center; CMMC, Hibbing; Dec. 16; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.

### January, 1981

**Winter Seminar; MN Academy of Family Physicians;** Puerto Vallarta, Mexico; Jan. 16-26; CONTACT Chari Konerza, Exec. Dir., MAFP, 8455 Flying Cloud Drive, Eden Prairie, MN 55344, 612/944-3585.

### February, 1981

**"Family Practice Review: Update 1981;** U of M Medical School; Radisson Hotel, St. Paul; February 2-7; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**"Adult Pharmacology";** U of M Medical School and School of Pharmacy; U of M Mpls.; February 18-19; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**"Practical Otolaryngology Update";** U of M Medical School; L'hotel de France, Mpls.; February 27-28; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### March, 1981

**"Annual Psychiatry Update";** U of M Medical School; U of M Mpls.; Mid March; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**"Sports Medicine Symposium";** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; March 20; CONTACT Glenn Gostick, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Seminar for Directors of Medical Education;** MMA; Spring Hill Center, Wayzata; March 27-29; CONTACT Teresa Rogstad, Rm 400, 2221 University Ave. S.E., Mpls., MN 55414, 612/378-1875.

For further information on the above or future CME programs, contact Teresa L. Rogstad, Director, Department of CME & Program Services, Minnesota Medical Association, Suite 900, American National Bank Building, 101 East 5th Street, St. Paul, Minnesota 55101 (612/222-6366).

**Minnesota Medical Association  
128th Annual Meeting  
May 20-22, 1981  
Radisson South Hotel  
Bloomington, Minnesota**



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Placement of ads by telephone not accepted. We also reserve the right to decline or withdraw advertisements at our discretion. Every care is taken to avoid mistakes but responsibility cannot be accepted for clerical or printers errors.

Cancellation of ads must be made before the 10th of the preceding month's issue.

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FAMILY PRACTICE opportunities in outstanding Southern Minnesota Group. The Albert Lea Clinic, P. A., is interested in contacting physician candidates for city and small town branch practices. This group is a 16 man multispecialty group in the primary and secondary care fields. Top salary first year. Senior physician participation beginning at the end of the first year, in incentive income distribution plan. Low cost buy in. Maximum profit sharing plan. Top level insurance plan and full range of other benefits. New hospital in city. Albert Lea is an exceptional place to live and these are choice practices. Please contact B. J. Boss, Administrator, Albert Lea Clinic, P. A., 1602 Fountain St., Albert Lea, MN 56007, Phone 507-373 8251, personal phone 507-377 1406 or contact Gary Boeke, M.D., 507-373 8251, personal phone 507-826-3288.

FAMILY PHYSICIAN needed to join a 10 member multi-specialty group in Southern Minnesota. Fairmont is a progressive city of 13,000 with excellent schools and recreational areas around a chain of five lakes. New 114 bed hospital adjacent to clinic. First year salary guaranteed with full partnership after one year. Contact Don Grandgenett, Fairmont Medical Clinic, PA Fairmont, MN 56031. (507) 238-4263.

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# President's Letter

## Professional Competence

All professions aspire to assure those they serve that they will be competently served. It is difficult, however, to determine and evaluate the competency of individual members of a profession, such as medicine.

Competence is hard to define. It reflects diverse components including native ability, knowledge, training, and experience. It is affected by an individual's ethics, integrity, and even his personality.

Fifty years ago if a physician received his doctorate from a recognized medical school, completed an internship, and was licensed by a state board of medical examiners, he was generally considered competent to practice as long as he wanted to. It is true that medical knowledge was expanding far less rapidly then than now, but undoubtedly that assumption was not always correct even at that time.

Subsequently residencies and fellowships in various medical fields developed. Individuals often were certified or boarded in these specialties and generally were considered competent because of the training and certification thereafter.

The need for continuing medical education has become increasingly apparent in recent years. Opportunities to obtain such education in various ways have expanded. Most physicians have utilized these opportunities.

Nevertheless concerns have developed both from within the profession and from outside that undergraduate, graduate, post graduate, and continuing medical education in itself does not assure professional competence. Although many approaches have been tried and suggested, it is clear that all have significant weaknesses.

Mandatory continuing medical education to retain licensure by a state, as in Minnesota, or to continue membership in a professional organization as required by the American Academy of Family Practice is certainly not the answer. Registration and even attendance can be monitored, but there is no way to assure acquisition of knowledge nor to assure its utilization in the individual's practice.

Voluntary self assessment examinations, if conscientiously employed, are undoubtedly valuable for some individuals, but are probably not generally satisfactory tools to assure competence.

Relicensure and recertification in a specialty can assess stores of knowledge as the original examinations did, but they are limited in evaluation of the application of that knowledge.

Auditing of physicians' office and hospital practices by peers either from the same community or from the outside probably comes the closest to fairly evaluating professional competence; however, even this approach has drawbacks including personal biases, both favorable and unfavorable, as well as the time and expense involved.

The evaluation of professional competence deserves additional thought and study. It is too early to be locked in to any of the approaches thus far considered. The action of the House of Delegates of the American Medical Association in July 1980, calling for a moratorium on mandatory relicensure and recertification of physicians deserves our support.



John K. Meinert, M.D.  
President  
Minnesota Medical Association



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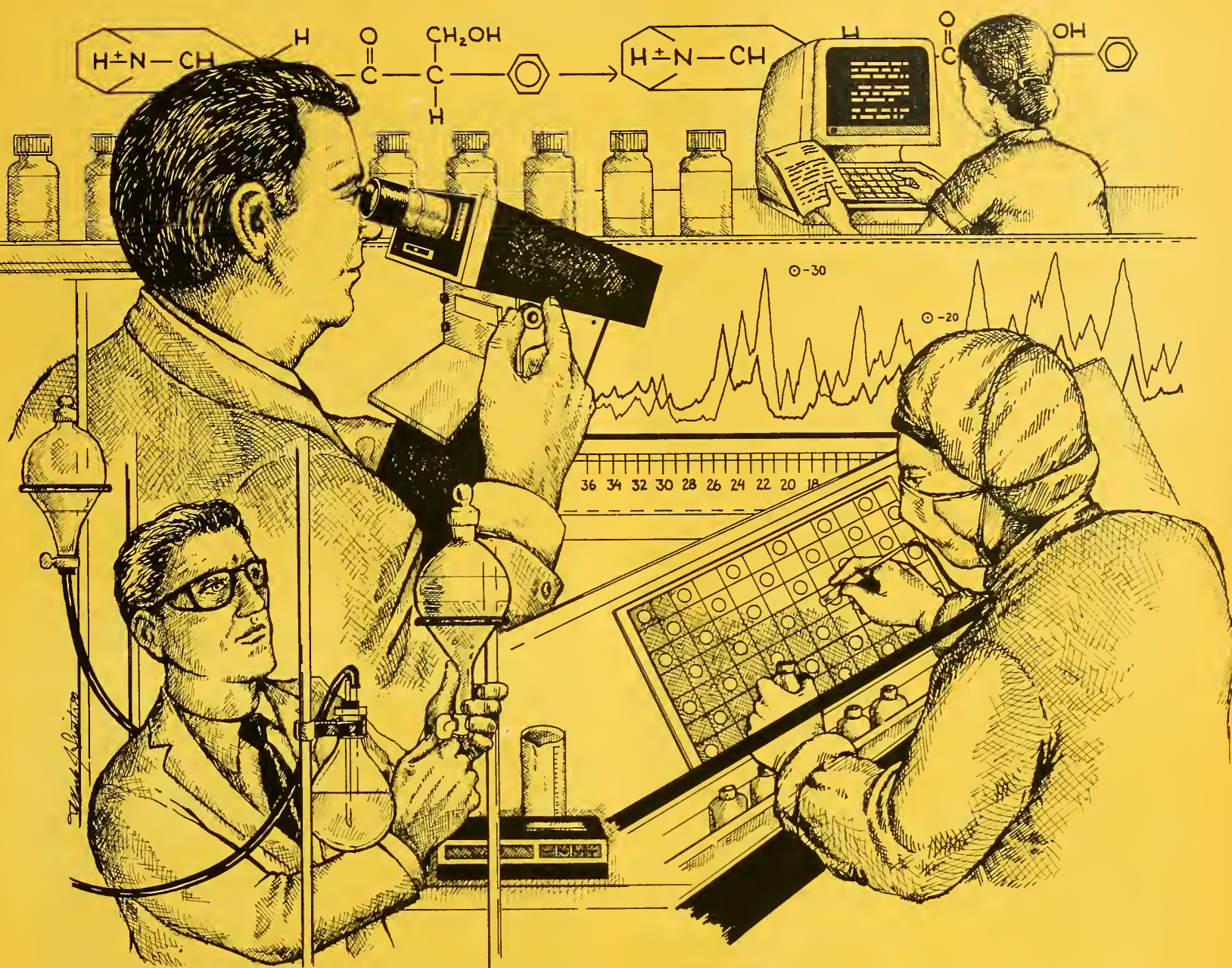
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# Book Reviews

**HOW TO BEAT FATIGUE** by Linda Pembroke, Doubleday and Company, Inc., Garden City, New York, 1975, 223 Pages. \$6.95.

This is another of those do-it-yourself books directed toward the recognition and cure or alleviation of a host of maladies ranging from alcoholism to premenstrual tension. Fatigue, defined variously as human inadequacy or a personal reaction to self-assessment, is one of those universal symptoms, like pain, and does not permit easy grasp without qualifiers.

Much of the text is carefully constructed and provides specific insights and suggestions to aid the lay reader in the recognition of those situations producing abnormal or disabling fatigue states. The section discussing life priorities taken from a book by Alan Lakein, and the chapter on sleep are well done and informative. The discussion of sleep stages, REM sleep, and dream states will enlighten and fascinate the casual reader. The sections on stress and mental depression are impressive, but probably of little value to the uninformed reader. Obesity, drug abuse, and alcoholism are introduced for completeness.

The position and value of this piece, and the many others of this genre, raises serious questions for this reviewer. The authors bring no expertise of their own, they borrow, quote and abridge the basic material and research. This kind of writing suggests spoon feeding of a pre-digested pabulum, not by a motivated mother, but at the whim of the babysitter. The bibliography alone, if pursued, may be value received. In this instance, of approximately ninety references, almost half are taken from newstand periodicals, and thus freely accessible at any local library.

**John V. Thomas, M.D.**  
Duluth, Minnesota

**GENETIC SCREENING. Programs, Principles and Research** by National Academy of Sciences. 388 pages.

This book is an excellent dissertation on the problems involved in genetic screening. It should be suggested reading material for anyone interested in setting up a genetic screening program. A detailed discussion of the problems of a registry in genetic screening is presented. This includes the maintenance of confidentiality, who should have access to the information on them and to whom this information should be released. Other areas highlighted by the book are those of personal and family responsibility that result after genetic studies have been performed.

The book goes into detail giving results of previous genetic screening programs which have been carried out such as the national program of phenylketonuria and the localized program in Baltimore, Washington area for Tay-Sacks disease. The results of these screening programs, the family or personal response to the screening programs and use of the screening results in counseling are discussed. It is pointed out that genetic screening programs must be coupled with genetic counseling programs. The genetic counselors must be people very well versed in the genetic disease for which they are counsel-

ing including risk factors, rate of occurrence and possible occurrences in future generations. These counselors are physicians who are specially trained in genetics but can be other paramedical counselors. It is pointed out that the material must be well understood by the counselees in order to be of any real value in future planning. The genetic screening material must be presented to the counselees in a manner which will be knowledgeable to them so it will be useful to them in planning future childbearing.

I feel the book would be excellent reading for anyone planning to set up a genetic screening program, however, I do not feel that it has much usefulness for the average practitioner who is involved in routine practice. The introduction to the book carries a warning which I think is well stated since genetic screening has many facets available to it. I would like to quote this comment "The limit for characteristics to be screened will be set, therefore, by the usefulness of the knowledge gained, the costs of obtaining it, and its impact on the persons tested rather than the number of tests that can be devised."

**Peter Fehr, M.D.**  
Minneapolis, Minnesota

**POST-MORTEM** by David M. Spain, M.D. with Janet Kole. Doubleday & Company, \$7.95, 296 pages.

Post-Mortem, a rather drab title, belies the content within. Dr. Spain has beautifully written with intrigue and mystery some of his experiences in solving murders, suicides, violent accidents, criminal abortions, and infanticides. He has done this by meticulous observation at autopsies of victims, along with careful, conscientious and understanding conferences with relatives and friends of the deceased.

Though individual personalities have been disguised, the facts and circumstances are true and historic. Some of the circumstances of the Chicago Shoot-Out and the trial of the New Haven Panthers, when read in the light of the news reports that many of us were no doubt aware of, give a different interpretation than that which we might have remembered from the sometimes biased news media.

Despite the fact that there were occasions in which Dr. Spain seemed unduly pessimistic, I was intrigued with his sense of humor. On one occasion when he had been asked to appear on a night-time television show to present his views with regard to tobacco as a cause for lung cancer, his young son, Robby, almost prophetically offered his own holster and guns to be taken along "The network wouldn't permit him to go on because the tobacco industry had a large investment in television advertising."

They apparently continue to censor out items derogatory to their own interests, but seem to encourage repetitious, character-assassinating news items that may be damaging to others.

Reading Post-Mortem was as fascinating as a mystery novel.

**Carl O. Rice, M.D., Ph.D.**  
Editor Emeritus



# Asymptomatic Space Occupying Lesions of the Kidney\*

ERICH K. LANG, M.D.†

**A**SYMPTOMATIC SPACE occupying lesions of the kidney are encountered in almost 20% of older male patients but are recognized in only 0.4% of a general hospital population.<sup>1,2</sup> This disparity in incidence is based on the established increased occurrence of renal cysts in older patients, and the increased utilization of high dose intravenous urography aided by tomography, in the workup of all older male patients admitted for symptoms related to the lower urinary tract or prostate.<sup>1,3</sup>

A 5% incidence of malignant neoplasms in our series of asymptomatic space occupying lesions of the kidney (Table 1) emphasizes the need for diagnostic assessment of all such lesions.

TABLE 1

Pathologic Diagnosis of 1350 Asymptomatic Space-Occupying Lesions of the Kidney

Cysts (65%)	887
Benign simple	856
Compound (multilocular)	8
Polycystic	16
Cystic dysplastic components	3
Hemorrhagic cysts	4
Malignant Neoplasms (5%)	67
Primary renal	26
Metastatic to kidney	41
Benign Neoplasms (4%)	58
Inflammatory Lesions (18%)	243
Hematomas (.3%)	4
Columns of Bertin (-7%)	91

The alarming frequency of asymptomatic renal masses and the age, general condition and risk of complications associated with diagnostic procedures in this group of patients call for a management protocol that is cost-effective and capable of establishing the diagnosis by the least invasive methods.<sup>1,2,4,5</sup>

## Diagnostic Approach

The proposed protocol deploys a minimum number of the least invasive procedures in a sequence that assures a confident diagnosis (Table 2)<sup>1,2,4,5</sup>. In the vast majority of patients, the diagnosis can be

established by two non-invasive examinations; only in a few will a third and more invasive procedure be necessary (Tables 2 and 4). The principal reason for this is the predominance of renal cysts and renal pseudotumors both of which account for 72% all asymptomatic renal masses (Table 1).

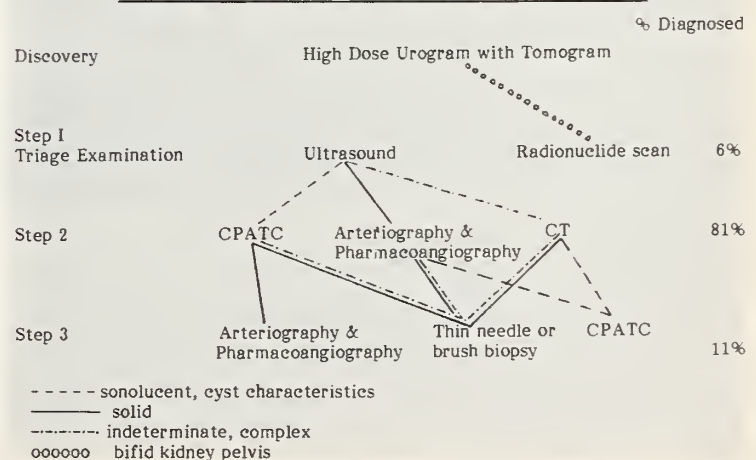
A bifid or duplicated collecting system splayed by a mass, most often presenting between the superior and middle calyceal groups, suggests the diagnosis of a renal pseudotumor. A radionuclide scan using 99m technetium DTPA or other agents that are concentrated in renal tubules together with an urogram showing the characteristic findings described above confirms the diagnosis of prominent column of Bertin (Tables 2 and 5).

Renal cysts are the most common lesion presenting as an asymptomatic mass (Table 1). The diagnosis can be made confidently using ultrasonography and the cyst puncture and aspiration test complex<sup>1,2,6</sup> (Tables 2 and 4). The computed tomogram offers criteria (sharply demarcated, spherical mass with low attenuation coefficient; failure to enhance after administration of contrast medium) that establish the diagnosis of renal cyst with high sensitivity and accuracy.

In this protocol, ultrasonography is advocated as the principal triage examination to differentiate between cystic and solid lesions. While the characteristic finding of a sonolucent mass with accentuation of

TABLE 2

Systematized Approach to Asymptomatic Space-Occupying Lesions of the Kidney



\*Presented as the Russell D. Carman Lecture at the Annual Meeting of the Minnesota Radiological Society, September, 1977.

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echoes from the far wall is diagnostic of a cyst, further investigation by the cyst puncture and aspiration test complex may supply information that predicts the probability of subsequent enlargement or regression of the cyst, and the presence of associated inflammatory or neoplastic disease.<sup>1,2,6</sup> The cyst puncture and aspiration test complex combines roentgenographic documentation of the lesion, visual assessment of the aspirate, histochemical assessment of the aspirate for tumor and inflammatory byproducts, cytologic assessment for neoplastic cells, and recording of the opening pressure existing within the cyst, criteria which permit assessment of the type, age and probable fate of the lesion with an unusually high degree of accuracy.

Percutaneous cyst puncture can be carried out under fluoroscopic or ultrasound guidance using a 20 gauge thin wall needle connected to a malleable tubing. A translumbar entry facilitates an angled approach to lesions in the upper pole of the kidney and thus prevents inadvertent puncture of the lung contained in the costophrenic sulcus.<sup>7</sup> The use of a malleable tubing

attachment allows free respiratory excursion of the needle without the danger of inadvertent parenchymal tear.<sup>7</sup>

The opening pressure in the cyst is recorded manometrically. The cyst aspirate is assessed visually for color, turbidity and blood content, histochemically for fat, protein, amylase, lactic acid dehydrogenase (LDH), glucose, urea nitrogen, and sodium content; and cytologically for malignant or inflammatory cells. The aspirate is then replaced by an aliquot of contrast medium and air.<sup>1,2</sup>

Decubitus, anterior, posterior, upright, and oblique views are obtained to document all inner surfaces of the cyst. Superimposition of the opacified cyst upon the negative defect seen on the tomogram obtained during the nephrographic phase of the high dose urogram serves to affirm that the entire lesion is adequately explained.

Benign cysts yield clear, straw colored fluid of low fat, protein, LDH and amylase content.<sup>1,2</sup> An opening pressure of 100 millimeters of H<sub>2</sub>O, a glucose content higher than the concomitant blood glucose level, a urea nitrogen content greater than 40 milligram percent and a sodium content greater than the concomitant blood sodium level indicate a cyst that is prone to expand, reform, and therefore, is capable of causing pressure atrophy of parenchyma (Table 3). Conversely, an opening pressure of less than 60 millimeters of water, a glucose content lower or equal to simultaneous blood glucose level, a urea nitrogen content lower than 40 milligram percent and a sodium level less than concomitant blood sodium level favor a cyst destined for spontaneous regression (Figures 1a and 1b).

Cystic or necrotic tumors or tumors within cysts generally yield a murky aspirate with high fat, protein, LDH, and elevated amylase content. Neoplastic cells are readily identifiable on cytologic examination performed on the filtrate enriched on a micropore

**TABLE 3**  
**Criteria for Predicting Disappearance**  
**Versus**  
**Enlargement of Renal Cysts**

	<u>Enlarging Cysts</u>	<u>Disappearing Cysts</u>
Opening pressure	≥ 60 mm H <sub>2</sub> O	≤ 100 mm H <sub>2</sub> O
Glucose content <u>blood</u> cyst fluid	1 or smaller	1 or greater
Urea nitrogen content	> 40 mgm %	< 40 mgm %
Sodium content <u>blood</u> cyst fluid	1 or smaller	1 or greater

**TABLE 4**  
**Percentage of Cases Diagnosed with Confidence**  
**by Proposed Protocol**

<u>Discovery</u>		<u>High Dose Urogram with Tomogram</u>	
Step I		Ultrasound	Radionuclide Scan (column of bertein 6%)
Step II	CPATC (cyst 63%)	CT (cysts > 1%) (benign tumors > 1%) (malignant tumors > 1%) (inflammatory lesions 2%) (hematomas > 1%)	Arteriogram & Pharmacangiogram (malignant tumors > 3%) (inflammatory lesions > 10%) (benign neoplasms 2%)
Step III	Arteriography & Pharmac- angiography (inflammatory lesions > 1%) (malignant neoplasms > 1%)	CPATC (cyst 1%)	Thin needle or brush biopsy (benign neoplasms 1%) (inflammatory lesions > 6%) (malignant neoplasms > 2%) (column of bertein > 1%) (hematomas > 1 %)





Fig. 1a — Tomographic cuts obtained in the urographic phase of an intravenous urogram demonstrate a parapelvic mass indenting the pelvis and displacing and splaying the infundibula of the superior and middle calyceal groups.

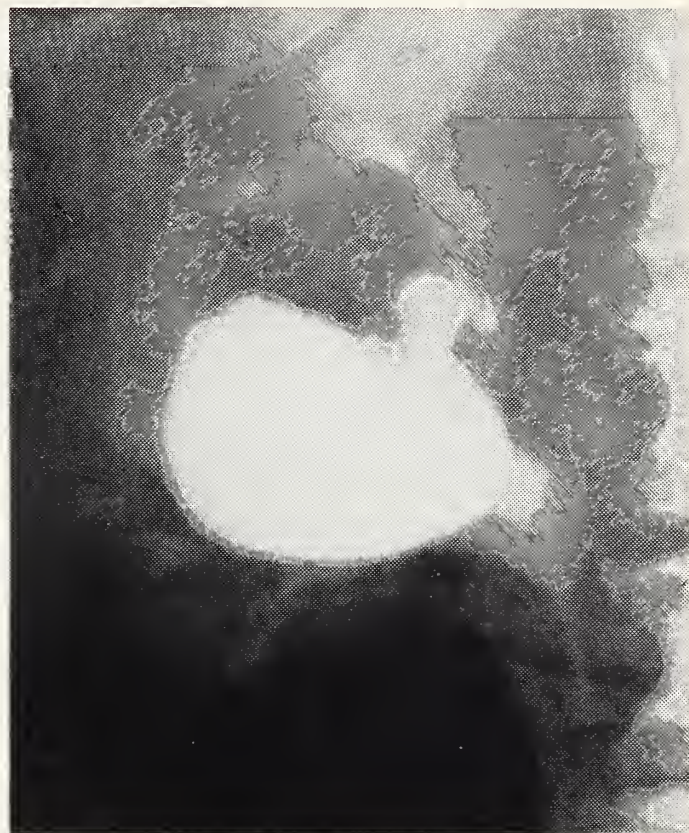


Fig. 1b — Cyst puncture and aspiration demonstrated a classical parapelvic cyst with an opening pressure of 40 millimeter of water, a glucose content 10% lower than simultaneous blood glucose level but a relatively high cholesterol content characteristic of parapelvic cysts. As predicted by the low glucose content and low opening pressure, the cyst regressed spontaneously and a followup examination six months later showed no evidence of a residual parapelvic cyst.

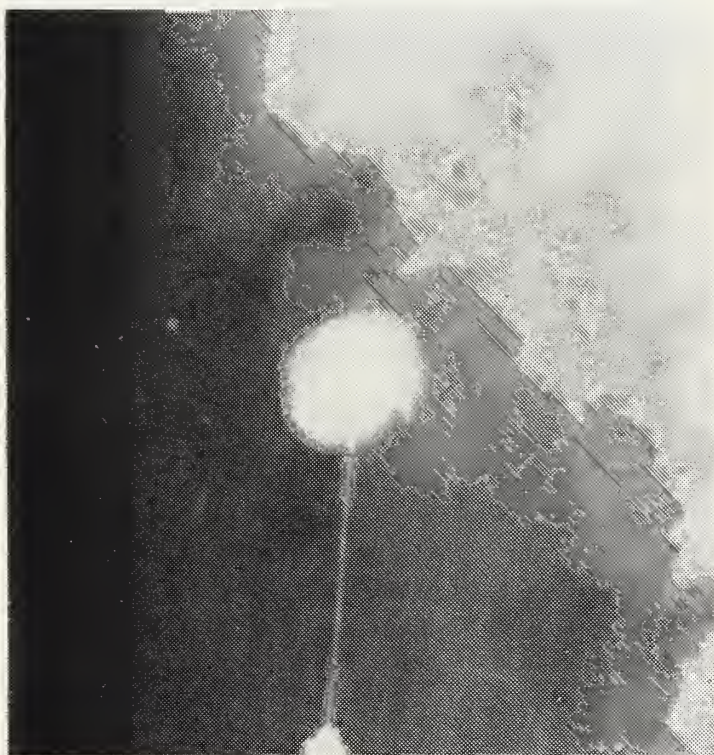


Fig. 2a — The aspirate from this cyst is murky in appearance. The double contrast study shows multiple filling defects and an irregular contour of the cyst wall.



Fig. 2b — Note subseptation in this cystic lesion and obvious nodular filling defects protruding into the lumen of the cyst. The appearance is characteristic for a cystic necrotic tumor. Fat and protein contents as well as the LDH level of the aspirate were markedly elevated.



filter.<sup>1,2,6</sup> Nodules protruding into the lumen of the cyst may be demonstrable on double contrast cyst study. Superimposition of the opacified cyst upon the negative defect seen on the nephrotomogram may identify unaccounted for components of the lesion which may prove to be solid or necrotic tumor components (Figure 2a and 2b).

Inflammatory cysts may yield clear, murky, or bloody aspirate with slight elevation of fat and protein content but significant elevation of the amylase and LDH levels. Inflammatory cells may be identifiable on cytologic examination, sometimes however, the cells may be of an indeterminate grade.<sup>2</sup>

Hemorrhagic cysts yield murky aspirate with high fat, protein, amylase and elevated LDH contents. The diagnosis is best made on basis of cytologic examination of the debris demonstrating acellular particulate debris and an abundance of cholesterol clefts (Figure 3). Double contrast studies show multiple filling defects attributable to fibrin or blood clots adherent to the wall of such cysts. Brush or aspiration biopsy or surgical exploration will frequently become necessary to exclude neoplastic disease with confidence.

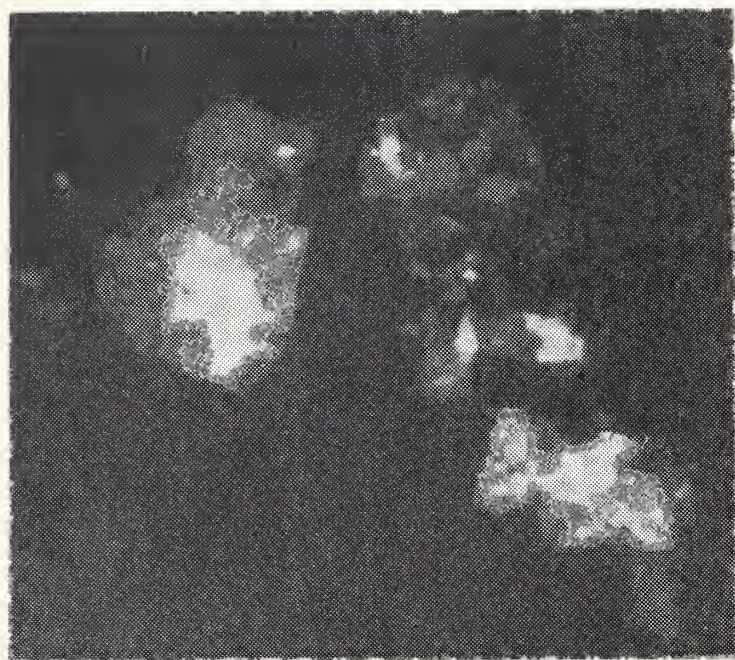


Fig. 3 — Examination of the debris aspirated from a cyst in polarized light demonstrates the classical reflectile cholesterol crystals. This is considered a strong criterion suggesting the diagnosis of hemorrhagic cyst.

Murky or necrotic material may also be aspirated from an abscess and bacteriologic studies are therefore indicated on such aspirate.

Failure to aspirate fluid (a dry tap), after properly affirming position of the tip of the needle in the center of the lesion, indicates the presence of a solid lesion. Suction, core aspiration, or brush biopsy may establish the precise diagnosis on basis of the cytologic substrate.<sup>2</sup> Injection of contrast medium into the lesion

may show a characteristic distribution pattern, such as, for example, for necrotic hypernephroma<sup>8</sup> (Figure 4).

Because of the preponderance of cysts and pseudotumors, the diagnosis is established by the combination of either ultrasound and the cyst puncture and aspiration test complex or ultrasound or a radionuclide scan in about 70% of this group of patients (Table 4).



Fig. 4 — Injection of contrast medium into the center of a lesion from which no fluid could be aspirated demonstrates a circoid distribution pattern characteristic for a necrotic hypernephroma.

If ultrasound suggests a solid mass (interface echoes elicited from within the mass and attenuation of sound transmission through the mass), arteriography or computerized tomography are advocated for further evaluation (Table 2).

The demonstration of tumor vessels, i.e., vessels of rapidly changing caliber on angiograms or particularly pharmacoangiograms, establishes the diagnosis of renal cell carcinoma.<sup>1,3</sup> Encasement of vessels, amputation of segmental or interlobar vessels and loss of interface between lesion and adjacent renal parenchyma may be found with squamous carcinoma, chronic inflammatory lesions, some metastatic lesions and rarely with transitional cell carcinoma. Occasionally pharmacoangiography may disclose a tell-tale neovascularity in the renal pelvis indicative of the diagnosis of transitional cell carcinoma. Although diagnosis by angiography is less specific than that by the cyst puncture and aspiration test complex, even a presumptive diagnosis of neoplasm serves the purpose,



since subsequent exploration or thin needle or brush biopsy will establish a definitive diagnosis. The angiographic findings in certain chronic inflammatory lesions (pruning and amputation of interlobar and tertiary vessels attributable to cicatricial changes) may closely mimic those of squamous cell carcinoma. A loss of definition of the interface between cortex and medulla and between the lesions and adjacent parenchyma, observed in the late arteriographic phase is likewise common to both lesions. The definitive diagnosis, therefore, often rests on cytologic diagnosis based on core aspiration, brush biopsy or open exploration. Table 4.

Acute inflammatory lesions tend to show hypervascularity in the rim of the lesion. Contrary to the hypervascularity of neoplasm, these vessels show orderly dilatation. Abrupt caliber changes, arteriovenous shunts or puddling of contrast medium are not seen.<sup>9</sup> Supply from extrarenal sources may be identifiable. The circulation tends to be sluggish, reflecting venous hyperaemia.

Computerized tomography is recommended if ultrasound demonstrates a complex or indeterminate pattern. Certain benign tumors like angiomyolipomas and lipomas can be diagnosed on basis of characteristic absorption coefficients.<sup>10,11</sup> Multilocular cysts are likewise readily diagnosable by CT. Even certain inflammatory lesions, abscesses and intrarenal hematomas can be diagnosed on basis of a characteristic change of absorption coefficients documented on sequential computerized tomograms.<sup>10,11,12</sup>

In 87% of the patients, the diagnosis is made with acceptable confidence by two methods of examination (Table 2). In 73% of the patients, the diagnosis is established at an unusually high confidence level by the combination of one or two non-invasive studies, i.e., ultrasound and a radionuclide scan, ultrasound and cyst puncture and aspiration test complex or computerized tomography. Only in the remaining 14% of the patients, is a more invasive study, arteriography, used. Yet, the diagnosis in this group is reached with lesser certainty, reflecting the lesser specificity of angiographic findings.

By adding a third study, the diagnosis can be made with acceptable confidence in another 11% of the patients.

Thin needle biopsy, core aspiration or brush biopsy are relatively new techniques yielding definitive diagnostic information. Percutaneous puncture is readily performed under fluoroscopic, ultrasound or CT guidance. Core aspiration or brush biopsy are

favored over thin needle biopsy since they allow a histologic rather than cytologic diagnosis (Figure 5). These techniques have been particularly useful for investigation of solid masses revealed by cyst puncture, or masses with indeterminate characteristics on arteriograms and computerized tomograms.



Fig. 5 — A nylon brush is introduced through an 18 thin walled needle into a solid mass in the left supra-renal space. Nitrous oxide is utilized to delineate the mass (arrows). Gas is favored over hypertonic contrast media to minimize distortion of cells for the cytologist.

In a few cases, cysts are diagnosed with certainty on arteriograms or computerized tomograms.

In a few patients, angiography is used as the third procedure if and when the cyst puncture and aspiration test complex or computerized tomogram indicate the presence of a solid but otherwise undetermined mass. In general however, thin needle biopsy has become the procedure of choice since it establishes the diagnosis in these questionable cases with confidence and utmost expediency.

One can also perform a thin needle suction or core biopsy first, and then utilize the sheath of the needle for the introduction of a nylon brush to retrieve multiple samples of cytologic material from several levels of a lesion.

### Summary

The proposed sequential diagnostic protocol for asymptomatic space occupying lesions of the kidney



offers a cost-effective approach to the management of these patients.

Seventy-three percent of all lesions are diagnosable by one or two non-invasive methods (cystic mass lesions and masses representing prominent columns of Bertin.)

Another 14% of the lesions, specifically malignant neoplasms, inflammatory mass lesions and some benign neoplasms are also diagnosable by a combination of only two examinations, ultrasound and arteriography. However, arteriography is considered a more risky and invasive procedure in this age group.

Finally, another 11% of the patients can be diagnosed by adding a third examination, i.e., computed tomography, guided thin needle, core aspiration, or brush biopsy. The latter modalities offer diagnosis by histologic or cytologic criteria and are, therefore, valuable in the definitive diagnosis of certain malignant and benign neoplasms, hematomas, inflammatory lesions and abscesses (Tables 2 and 4).

About 2% of the patients proved refractory to this diagnostic approach and had to be explored. The increased availability of guided thin needle, core aspiration or brush biopsy, however, is expected to obviate the need for surgical exploration in the future.

The accuracy of diagnosis varies with various entities and is the highest with renal cysts. Moreover,



Fig. 6 — A computed tomogram demonstrates a sharply demarcated, mass in the midpole of the right kidney which fails to enhance after administration of the contrast material. The attenuation coefficient is measured as plus five. All criteria of a benign cyst are met by this appearance.

certain biochemical criteria predict the probability of subsequent enlargement or regression of the cyst, and in the former case, the necessity for measures to preserve renal parenchyma. If an enlarging cyst is suggested, sclerosing agents can be introduced through the puncture needle into the cyst, for therapeutic purpose.

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# Chronic Pain — Fact or Fiction

DAVID W. FLORENCE, M.D., M.A.P.A.\*

TEN YEARS AGO if you would have asked me the definition of chronic pain, I probably would have responded with a profound statement such as "pain that won't go away". Today that magnificent comment may still hold true, but for those of us who have been pushed into the back door of the chronic pain arena, the words "chronic pain" take on a new significance.

The recent emphasis was precipitated by that infamous entity called "the bottom line". Varying statistics are picked up in the literature and at chronic pain seminars, and all of them are reasons for concern. John J. Bonica, M.D.,<sup>1,2</sup> one of the pioneers in chronic pain management, stated in his keynote address at the Second Annual Conference on Chronic Pain at Emory University, in May of 1978, that "chronic pain syndromes cost the American people between 40 and 50 billion dollars annually". From the aspect of low back pain alone, there are estimates of annual expenditures of 12 billion dollars. This would include health services plus loss of work productivity. Two billion are spent annually on workmen's compensation payments to low back patients alone.

The most startling revelation was the realization that the major portion of this expenditure was for chronic pain — not acute care management.

So what is chronic pain? Well, chronic pain is a combined medical, legal and social problem; medical in that the doctor is supposed to solve the problem; legal in that the process of disposal of the patient is through statute and judicial dictates; social in that the end result affects each one of us either directly or indirectly; directly, in that all of us pay the ultimate bills through our tax structure or the products we buy; indirectly, in that most chronic pain patients end up in divorce or insolvable marriage problems, and suicide is seen in a proportion well beyond the standard norm for population of a similar age and sex.

It is important for physicians to differentiate between disability and impairment. Disability is a legal term which means the inability to perform activity by means of impairment. Impairment is a medical term which means a reduced level of health or wellness,

either from physical or mental causes. Chronic pain itself is an impairment, well recognized by algologists (pain specialists) as a perception — not a sensation. It can neither be localized nor surgically removed. In fact, Benjamin L. Crue, M.D.,<sup>3</sup> the neurosurgeon and former director of the City of Hope Pain Center, in Duarte, California, frankly stated that "chronic pain is not a surgical condition; in fact, it does not respond to surgery."

A typical feature of chronic pain is that it persists without peripheral input. In other words, it is self-perpetuating. The pain occurs in the higher central nervous system areas and does not respond to standard medical treatment modalities. This should be no surprise to any physician in that all of us accept the concept of phantom pain, which in reality is a form of chronic pain. Improvement of phantom pain is rarely seen from surgical intervention, be it limited or extensive.

We have all come to recognize that chronic pain patients are different. Besides not responding to most standard care, be it medical or surgical, certain general characteristics are seen. The patients tend to dwell or develop a fixation on their trauma or "accident", as in the case of workmen's compensation problems. Certain anxiety and hysterical features become paramount and are consistently seen in the MMPIs of such patients. However, it is possible for a chronic pain patient to have a normal MMPI. Denial of the problem is almost as prominent a feature as is seen in alcoholism. In any case, these patients ultimately lose their ability to "cope" with life, particularly on a daily basis. For one reason or another, they are programmed or conditioned for disaster.

Specifically, these patients usually reflect a picture of the six Ds: (1) Drug abuse; (2) Disuse; (3) Dependency; (4) Depression or anxiety; (5) Disability as a self-concept; (6) Doctor usage.

At our treatment center, approximately 40% of the patients admitted have an addiction problem to medications, ranging from mild to severe. The majority of these medications have been doctor prescribed (iatrogenic). Many have been on medications for years, frequently receiving such from multiple sources.

The majority of the patients have been on

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“prolonged rest”, an integral part of the triad of rest, physical therapy, and pills. Most are actually in a catabolic state with extremes occasionally seen, such as generalized osteoporosis without a systemic etiology.

The vast majority of the patients are of a dependent personality type, or are independent persons addicted to medication and/or alcohol (usually for the purpose of pain relief).

Depression is more commonly seen than not, or is substituted by an anxiety state — the former leading to further inactivity and the latter to a state of exhaustion.

The mental frame of disability becomes a permanent personality feature with a concomitant loss of self-concept and self-approval. A feeling of worthlessness is not uncommon. At this point the entire family is profoundly affected.

The final category of the six Ds is the multiple and relentless use of doctors, many of whom run the same tests and do the same operations over and over, without any sustained relief.

Once the realization of a chronic pain status of a patient is recognized, what can or should be done? It has been our own experience that the true chronic pain patient cannot usually improve unless totally removed

from the enabling atmosphere. This means putting the patient into a pain treatment center. So what is a “chronic pain center?” As expressed by Benjamin L. Crue, M.D., again in the Second Annual Chronic Pain Conference at Emory University, “A pain center is whatever you want it to be.” In other words — whatever works for you and your staff and makes the patient well again. At the same conference, Dr. Steven F. Brena, Director of the Emory University Chronic Pain Center, responded to the question by stating that a pain center is “loving care on a structured basis.” This latter definition is the concept which I personally have chosen, realizing that others can be equally as effective.

In general, I feel that one must replace chronic pain with a substitute system. We at Sister Kenny have chosen intense physical and mental reactivation. Specifically the goals must be to decrease the perception of pain; increase bodily function; increase awareness of emotional aspects and give the patient tools to handle such problems; and ultimately get the patient back to gainful employment so that self-respect and self-worth are reestablished. The method is not the critical factor — the end result is.

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# Comparison of Glomerular Filtration Rate, Blood Urea Nitrogen and Serum Creatinine in Patients with Chronic Urinary Tract Disease

MARY PRICE, M.D.\* and FREDERIC J. KOTTKE, M.D.†

**T**HE NEED TO lower costs of medical care emphasized the importance of re-evaluating laboratory tests to see if cheaper procedures will provide the same information as expensive ones.

The glomerular filtration rate is a good indicator of early damage to renal function in patients with chronic urinary tract dysfunction because it has been shown that in such patients glomerular filtration deteriorates sooner than tubular excretion.<sup>1</sup>

For many years<sup>2</sup> the inulin clearance has been accepted as an accurate method of determining glomerular filtration rate. However, clearances are time consuming and expensive. Many clinicians depend instead upon the levels of blood urea nitrogen (BUN) and serum creatinine as measures of kidney function. How closely do the glomerular filtration rate, BUN and serum creatinine agree as indices of renal damage?

To answer this question BUN and serum creatinine were determined simultaneously with 1418 glomerular filtration rates. The glomerular filtration rate was determined by constant infusion inulin clearance using the Bojeson method of analysis.<sup>3</sup> The BUN was determined by the urease method<sup>4</sup> and the serum creatinine by the Jaffe method.<sup>5</sup>

Normal test values are: Glomerular filtration rate 72-176 ml/min/1.73M<sup>2</sup> (mean = 124); BUN 9-23 mg%; serum creatinine 0.5-1.0 mg%. Values represent a range of  $\pm$  two standard deviations from the normal mean which would include 95% of normal values.

The subjects of this study were spinal cord injured persons with chronic urinary tract pathology.

Ninety-two percent of the values for filtration rate (1304 of the 1418 tests) fell within the normal range. In

three of these tests (0.2%) the accompanying BUN was abnormally high, ranging from 24-28 mg%.

In 117 cases (9%) the serum creatinine was elevated, ranging from 1.1-6.5 mg%. In 43 tests, elevated serum creatinine which accompanied normal glomerular filtration rate occurred in the first year after injury when denervation and immobilization were resulting in atrophy of muscles.

In the 114 cases in which abnormally low glomerular filtration rates indicated decreased renal function, 76 were in the third standard deviation below the mean, between 46 and 72 ml/min/1.73M<sup>2</sup>; yet the BUN was normal in 86% of these tests while only 14% showed elevated BUN values, ranging from 24-32 mg%. Eighty-one percent of the accompanying serum creatinines had normal values, and 19% were between 1.1 and 1.6 mg%.

Even at glomerular filtration rates between 20-45 ml/min/1.73M<sup>2</sup> (the 4th standard deviation below the normal mean) only 34% of patients had high BUN values of 24-41 mg%. The serum creatinine was elevated to 1.1-3.8 mg% in 84%.

Three of the four tests in which the glomerular filtration rate was less than 20 ml/min/1.73M<sup>2</sup> were accompanied by abnormally high BUNs (25-45mg%). All four serum creatinines were elevated (1.1-3.8 mg%).

In instances of mildly depressed glomerular filtration rate, the values of serum creatinine and BUN were usually normal although the incidence of elevated serum creatinine was greater than BUNs, 20% compared to 4%.

When the glomerular filtration rate was moderately depressed, between 20 and 45 ml/min/1.73m<sup>2</sup> (the fourth standard deviation below mean) 84% of serum creatinines and 34% of BUNs were abnormally high.

In the four tests when the glomerular filtration rate was in the fifth standard deviation below normal, all serum creatinines were high and three BUNs were elevated.

In the series of 1418 studies of renal function using

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†Professor and Head, Department Physical Medicine and Rehabilitation, University of Minnesota, Minneapolis.

This study was supported in part by the University of Minnesota Medical Rehabilitation Research and Training Center, RT-2, under Rehabilitation Services Administration grant 16-P-56810/5-14.

Reprints from: Dr. Mary Price, Department Physical Medicine and Rehabilitation, Box 156 Mayo, University of Minnesota Hospitals, Minneapolis, MN 55455.



inulin clearance as the measure of glomerular filtration, neither blood urea nitrogen nor serum creatinine were reliable indicators of either normal or abnormal function until the abnormality became extreme. Serum creatinine gave nearly 10% positive tests in kidneys with normal glomerular filtration. When there was mild or moderate deterioration of renal

function neither BUNs nor serum creatinine gave reliable nor quantitative indication of the status of the kidneys. If it is important to know the status of renal function before the patient has far advanced renal dysfunction, then it is necessary to use a reliable clearance technique.

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#### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
3. Has made outstanding contributions to the Medical School, the University, the Alumni, and the community.
4. Has had a relatively long experience in the field of medical science or a related field.

Nominations for the March, 1981 awards should be sent immediately to:

Konald A. Prem, M.D., Chairman,  
Harold A. Diehl Award Committee  
Box 395, University of Minnesota Hospitals  
Minneapolis, Minnesota 55455  
(612) 373-7635

Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.

#### Continuing Medical Education St. Paul-Ramsey Medical Center

The fourth *Clinical Toxicology* Quarterly Update Conference will be held in The Gillette Amphitheater at St. Paul-Ramsey Medical Center on Wednesday, November 12, 1980. Speaker will be Dr. Anthony R. Temple, Director of Medical Affairs, McNeil Consumer Products. Subject of his talk will be "Iron Poisoning". Conferences qualify for Category I CME credits. Sponsored by the Emergency Medicine Department at St. Paul-Ramsey Medical Center and the University of Minnesota Medical School under the direction of Dr. Kusum Saxena. For further information please contact: Carol J. Wolf at (612) 221-3311.



# Rheumatology Corner

## Psoriatic Arthritis

J. MICHAEL CONDIT, M.D.\*

Arthritis coexists with psoriasis to a degree greater than that expected by chance alone. Initially this was believed to be due to the concomitant presence of two relatively common diseases, psoriasis and rheumatoid arthritis. Psoriatic arthritis has since been recognized as a distinct entity. The differential diagnosis of psoriatic arthritis includes rheumatoid arthritis, idiopathic ankylosing spondylitis, Reiter's disease, the arthritis of inflammatory bowel disease, osteoarthritis, chronic sarcoidosis, and gout.

Approximately 6-10% of psoriatic patients will develop arthritis. This usually follows the onset of skin disease, but the arthritis may precede the skin lesions and make the diagnosis more difficult. 70% of psoriatic arthritics have asymmetrical oligoarticular disease. Symmetrical polyarthritis resembling rheumatoid arthritis is seen in another 15%, but these patients have negative rheumatoid factors and no subcutaneous nodules. Arthritis mutilans is a severely destructive form of arthritis occurring in only 5% of patients and is characterized by "telescoped" digits and the "opera-glass hand". The remaining patients have ankylosing spondylitis or disease confined to the distal interphalangeal joints.

The correlation of arthritis with nail changes is stronger than that with skin changes. 80% of psoriatics with arthritis will have nail changes as opposed to 20% of psoriatics without arthritis. These changes are pitting, transverse ridging, subungual hyperkeratosis, onycholysis, yellowing and massive nail destruction. It has been claimed that arthritic joints are in geographical proximity to nail changes.

The most common radiographic abnormalities are marginal erosions of the interphalangeal joints in an asymmetrical pattern. Significant demineralization is rare. Other x-ray changes are acro-osteolysis, whittling of the distal ends of phalanges, the "pencil-in-cup" deformity, periostitis, and complete joint resorption. Radiographic sacroiliitis may be unilateral or bilateral, and spinal disease has a greater tendency toward "skip areas" than does idiopathic ankylosing

spondylitis.

CBC, urinalysis, and chemical profile are normal. Uric acid may be elevated with active inflammation. Rheumatoid factor and FANA are negative, and synovial fluid is usually inflammatory. There is a high incidence of HLA-B27 positivity in psoriatic arthritis with sacroiliitis.

Treatment of psoriatic arthritis begins with antiinflammatory drugs such as aspirin, indomethacin, tolmetin, or phenylbutazone. Intraarticular corticosteroid injections may be particularly useful when the disease is confined to one or few joints. Gold therapy or low doses of prednisone (5-10 mg/day) may be helpful with more severe arthritis. Hydroxychloroquine has recently been suggested for use as a remittive agent for typical psoriatic arthritis after years of concern regarding the potential of causing "skin flares". Arthritis unresponsive to conventional therapy may respond to aggressive treatment of the skin disease. Immunosuppressive agents such as methotrexate have led to improvement in both skin lesions and arthritis. Physical therapy may be helpful at any stage of the disease.

TABLE 1

Asymmetric Oligoarticular Disease	70%
Rheumatoid-like Disease (polyarticular symmetrical)	15%
Distal Joint Disease and/or Spondylitis	10%
Destructive Arthritis (arthritis mutilans)	5%

TABLE 2

Characteristic Features of Psoriatic Arthritis
Classical psoriatic skin and nail changes
Asymmetrical arthritis often affecting DIPs
B27-positive sacroiliitis
Correlation of arthritis with nail changes
Clinical and radiographic periostitis
Negative rheumatoid factor
Absence of subcutaneous nodules

\*Houston, Texas.



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Institutions and organizations seeking MMA cosponsorship for their CME programs (for AMA or LCCME Category 1 credit) may obtain information and application forms from:

Minnesota Medical Association  
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(612) 378-1875

Minnesota specialty societies that are represented on the MMA Interspecialty Council and have already appointed "CME Coordinators" to work with the MMA in cosponsorship relationships should have their coordinators submit application for cosponsorship at least 30 days in advance of the program date.

Other groups may be assigned an MMA representative as "CME Coordinator" upon approval by the MMA Subcommittee on CME Resources. This representative will participate in the planning process in order to assure that the criteria for Category 1 credit are met and will subsequently submit the application for cosponsorship. Request for a cosponsorship representative must be made at least 90 days in advance of the program date.



# Minnesota Medical Association Auxiliary

## An Update of Pre-School Medical Survey of Vision and Hearing

Mrs. Chauncey M. Kelsey

This valuable program of screening primarily four-year-old children for unrecognized possible problems of vision and hearing continues throughout Minnesota. Some MMA Auxiliary members volunteer as Screeners and as Demonstrators.

I would like to emphasize the value of the work done by the Auxiliary members. Probably the most outstanding aspect is the unique public relations. In working with the volunteers and the parents of the community, the Auxilian transmits a positive and improved medical image to the public. The Demonstrator is trained to teach the Screeners. Usually this training period is one day with a requirement of a retraining session annually. The Screeners must be trained by a qualified Demonstrator in order to maintain the high standards of this medically-oriented volunteer program. The rewards are great when one realizes the expanse of a four-year-old's learning through his/her vision and hearing.

At this particular time, the Auxilians again have been urged to familiarize themselves with the nature of this exceptional volunteer program which is endorsed by the MMA and financially supported by MSPB. This includes investigation of the present state-mandated Pre-School Screening. When examining the cost of the program, it has proven to be not cost beneficial. Also, there is a question whether referrals are made to health practitioners instead of to the family physicians.

May I urge each one to contact his legislator to scrutinize the value of the State's Pre-School Screening versus the Pre-School Medical Survey of Vision and Hearing, which is conducted by qualified volunteers at a minimal cost.

Our aim is to reactivate Pre-School Medical Survey of Vision and Hearing, to use volunteers in order to keep the costs controlled, and to see that the referrals are made to the children's personal physicians.

---

### Continuing Medical Education

University of Minnesota

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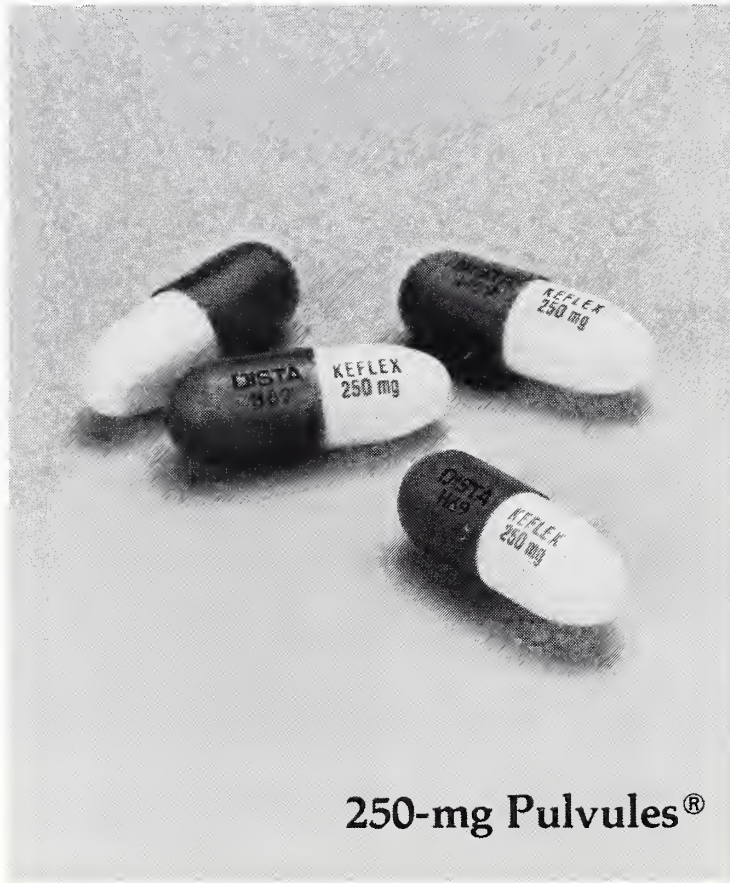
Location: Sheraton-Ritz Hotel, 315 Nicollet Mall, Minneapolis, Minnesota.

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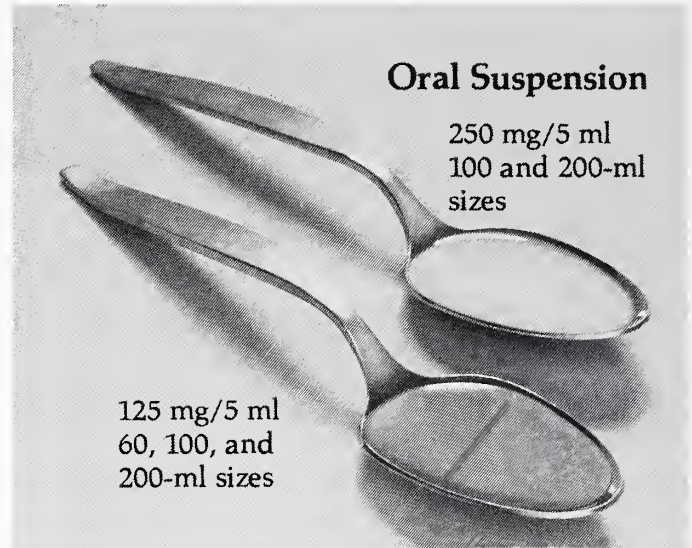
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# Address

## Tribute To a Wonderful Colleague, Teacher, Scientist, and Humanist Leo G. Rigler

OWEN H. WANGENSTEEN, M.D., Ph.D.\*

WE ARE MET today to pay our respects and a tribute to a Great Minnesotan, a former distinguished member of this medical faculty, and a wonderful friend, who influenced the lives of all fortunate to have been associated with him, Dr. Leo Rigler. Leo was born in Minneapolis, October 16, 1896 and died peacefully while asleep in his Los Angeles home, October 25, 1979, after having spent the morning at the U.C.L.A. Hospital.

When Leo became our university's professor of radiology, it was a relatively new medical discipline. The physicist Roentgen of the Würzburg faculty discovered the X-rays in 1895, creating a triumphant discipline for medicine. When Leo took over this new enterprise at Minnesota, July 1, 1927, he had a parttime technician in the person of Mrs. Lillian Dahl, also the departmental secretary. He and she constituted the department. Leo's part-time antecedent, Robert Glen Allison continued to give an occasional lecture. Radiology an erstwhile division of surgery, had very limited quarters and equipment in the Elliot segment of the hospital on level II; Leo's magnetic personality presently brought to the department many alert and promising trainees. How the department prospered under Rigler's leadership is well known far beyond the borders of Minnesota. In this very Amphitheatre 50 years ago, Leo began his weekly Saturday morning interdepartmental Radiology Conference, very novel then for this area: it proved so popular, Leo presently was performing similarly for virtually all medical disciplines. He added distinctions to every area of interest in which he took part.

On the advice of Dean Lyon, he completed an internship in 1921 at the St. Louis Municipal Hospital, where he spent much time with Dr. LeRoy Santé who greatly stimulated Leo's interest in radiology. April 4, 1979, 58 years after his internship at St. Louis Municipal Hospital, Rigler was privileged to give the first LeRoy Santé Lecture. Leo, in his 83rd year, began

by saying, King David and King Solomon had led very, very merry lives, but "when old age took them with many, many qualms, King Solomon wrote The Proverbs and King David wrote the Psalms." Leo obviously had become very conscious of the circumstance that maturity has a serious mien without time for frivolity.

After the St. Louis internship there followed a year in general practice in a small village in Hettinger County, southwestern North Dakota. The village named New England then could boast only 200 residents. Of that period in a letter of November 30, 1979, Leo's devoted and helpful wife of 53 years wrote, "To keep occupied and help augment Leo's meager income I taught in a Consolidated High School, every subject from drama, dance, and English, to geometry and zoology. Our intentions were to amass



Leo G. Rigler, M.D.

\*Regents' Professor Emeritus, Department of Surgery, University of Minnesota, Minneapolis, Minnesota.

Presented at Leo G. Rigler Memorial Service, December 12, 1979 in the Todd Amphitheatre, University of Minnesota Medical School.

A Search and Assessment supported by the Ralph and Marian Falk Research Foundation.



a small fortune of \$5,000 and Leo would then return to the University for a residency. Our one year in New England proved to be a financial failure."<sup>2</sup> The financial depression in agricultural midwest rural America began actually in 1921, eight years before the stock market crash of October 1929. Continued Matyl, "The last bills to be paid were doctor's fees, and more often than not were never paid at all."

After the year in general practice, Rigler returned to the University of Minnesota in 1922 and spent a residency of almost a year in internal medicine, followed by a similar period of time in pathology, which diversionary studies provided young Rigler with the broad orientation constantly reflected in his brilliant career in radiology. Much of 1924, Leo spent with J. T. Case pursuing his interest in radiology at Battle Creek and with the radiologist P. J. Hickey at the University of Michigan at Ann Arbor. Hilding Berglund came to Minnesota in 1925 as the University's full-time professor of medicine, supplanting S. Marx White, a half-time appointee; Berglund and Dean Lyon counselled Rigler to work for a year with Gösta Forssell in Stockholm, one of Europe's leading scholar radiologists. Leo became Forssell's first American student. Concerning Leo's work with Forssell, Matyl wrote, "Sweden perhaps the foremost center of radiology at that time had the greatest influence on Leo's career. Of all the pioneer greats, the distinguished and brilliant Gösta Forssell towered over them all. Tall, broad, handsome, a giant of a man in body and brain, he numbered among his patients many of the aristocracy of Europe. Dr. Forssell was both an inspiration to Leo professionally and a great friend and advisor to both of us."<sup>2</sup> That exposure quickened and intensified young Rigler's commitment to a life's career in radiology, and upon his return from Sweden in 1927, Rigler was made associate professor in his discipline; in 1929 at age 33, full professor, a position he filled with dignity and great distinction over a period of more than 30 years until retirement at Minnesota in 1957; he then became Director of the Cedars of Lebanon-Mt. Sinai Hospital in Los Angeles while serving as Chief, too, of radiology; soon thereafter, Rigler was made professor of radiology at U.C.L.A. with primary responsibility for instruction of radiological trainees. There Rigler had a second illustrious career, being recognized by the under-graduate student body twice as the School's finest teacher, for which achievement he was twice awarded the Golden Apple.

One reason for Rigler's phenomenal early success at Minnesota was appreciation of the fundamental pedagogic principle that the first obligation of the

professor is to create within his departmental sphere an atmosphere friendly to learning, a magnetic quality in which scholarship thrives, attracting earnest students from everywhere. In a commencement address to the 1965 graduating class in medicine at U.C.L.A., Rigler revealed the depth and breadth of his commitment and devotion to teaching. Said Leo, "I look upon you . . . the graduating class as our major claim to immortality . . . you represent both the ultimate justification for the existence of this faculty and the future of medicine."<sup>3</sup> If every member of our own faculty shared Rigler's dedication to teaching, what a heart-warming response it would evoke from our student body. In all medical schools throughout our great land, much attention has been paid student performance. In my view, it is high time that similar attention be devoted to teacher performance. On this score, from the very beginnings of his tutorial duties, Leo Rigler justly gained high marks. When teachers succeed in kindling fires of enthusiasm for learning, only then is the educational process well served.

Matyl also related in her letter that when Leo entered medical school, a teaching assistant in anatomy disapproving of his drawing of a frog said, "Young man, if this is the best you can do, you would be wise to give up medicine." Perhaps some of you too have heard such pleasantries from a misguided teacher.

Rigler also displayed during his early years at Minnesota a keen interest in keeping practicing radiologists over the breadth of our land up to date on innovations in the discipline. His was one of the best attended radiologic post-graduate courses in America.

The best measure of the success of all teachers is their intellectual progeny. On this score, Leo Rigler ranks among the highest. His many trainees in radiology occupy important posts amongst the best American universities, also in several foreign universities throughout the world.

A fundamental observation on the nature of the learning process is revealed in one of Ralph Waldo Emerson's essays. He told of his unsuccessful efforts in trying to push a calf into the barn. The Emerson maid, noting the proceedings through the kitchen window, came out, put a finger in the calf's mouth and the mission was quickly accomplished. Encouragement is truly a primary and significant ingredient in the learning process. Any teacher who discourages a student does a disservice to the educative process. Leo Rigler was a master in the Emersonian precept of encouragement.

In his retirement address of 1936 titled "Ave et Morituri Salutamus," Elias Potter Lyon, our third



medical school Dean, remarked that the greatest Dean he knew was Kipling's regimental water carrier, Gunga Din, a confession that all departmental Heads would do well to keep in sharp focus. A great opportunity in the academic arena is a mandatory summons to achieve, the only manner in which a youngster can repay his institution and society for the great privilege of superior opportunities early in his or her professional life, an obligation that Rigler, an unusually perceptive teacher, fully understood.

Lyon came to Minnesota in the first week of September 1913 at a time when Leo Rigler, aged 16, enrolled as a freshman at the University. Their destinies were to be intimately interrelated. In writing of the medical school that grew under Lyon's direction, Rigler rhetorically queried: "Who was the leader of this remarkable collection of personalities and talent known throughout the world, but assembled in this very small and little-known medical school in the Midwest, away from the usual crossways of travel?" Lyon obviously was Leo's hero too.

Lyon found our medical school in the midst of turbulent turmoil. George Edgar Vincent, our third university President and certainly one of our greatest, came in 1911 determined to turn around the face of our medical school from one of self-satisfied mediocrity, with most of its chairs occupied by part-time practitioners. When Vincent left in June 1917 to head the Rockefeller Foundation in New York City, the disturbed atmosphere at the medical school had quieted considerably. Through patient and compassionate understanding, Lyon succeeded in convincing many of Minnesota's practicing physicians that Vincent's faculty changes in the long run were all for the better, and in October 1917, William Mayo persuaded the State Legislature to approve the Vincent-Mayo proposal of an affiliation between the Mayo Foundation and the University's graduate school, an arrangement that has served the interests of both institutions very well. Leo was a medical student here during those troubled years and was witness to the medical school's gradual escalation to an institution of first rank before Lyon's retirement in 1936.

In the early 1930s, our medical school had the youngest clinical faculty in the country. Lyon had great faith in young persons of promise. To create professors of untried youngsters obviously involves risks, but Lyon had an unusual facility for recognizing talent. Rigler was one of the first amongst that group of young clinical appointees at Minnesota; others were Charnley McKinley in neurology, Irvine McQuarrie in pediatrics, Cecil Watson in medicine, John McKelvey in

obstetrics and gynecology, and Maurice Visscher in physiology who worked intimately with clinicians and especially with the department of surgery upon which he left a lasting impact. They, together with many Greats amongst the preclinical staff, also Lyon-appointed, were the true builders of the great name that the University of Minnesota Medical School justly earned over the years. Lyon was a keen judge of men and lent great encouragement to his young staff, a well-kept secret of successful pedagogy.

Under Rigler's direction, our department of radiology expanded greatly, developing sectional divisions of radiation therapy, neuroradiology, and nuclear medicine, functions greatly expanded upon in more recent years. Rigler's own work encompassed all facets of radiologic diagnosis, but his most significant contributions concerned the viscera of the two large body cavities, the abdomen and thorax. In both these areas, he made important observations that have withstood the erosion of time.

During his long and illustrious career, many radiological honors were bestowed upon Rigler; he was elected to honorary Fellowship in several international radiological groups, honored too by many American radiological societies and president of several; for long years, associate editor of *Radiology*; The author of several books on radiology and of more than 250 journal articles on radiological topics — reflecting a very busy and productive professional career.

A very recent letter from Professor Björn Nordenström<sup>6</sup> of the Karolinska Hospital relates that Leo's picture now hangs prominently on a wall in the Radiologic Institute beside that of Forssell and other Roentgen Greats of this century.

It has often been said that Leo Rigler trained more leaders for the radiologic academic arena than any radiologist of his time. It is primarily as Teacher and Innovator of a great School of Radiologists that we honor our erstwhile colleague today. Since Plato, a fourth-century B.C. contemporary of Socrates, taught in the Groves of Académie, it has often been stated that the effective teacher, more than anyone else, through his intellectual progeny is most likely to affect eternity. Of this mould in a discipline he helped build at Minnesota was Leo Rigler, "the father of modern-day radiologic diagnosis."

All privileged to have known this remarkable man, while mourning the departure of a great friend, will want to express appreciation for a dedicated life of toil amongst us for a man's betterment. In solemnizing this occasion by memorializing a great Minnesotan let us



also express our gratitude for a commendable and productive life appreciated by a host of patients, hundreds of students, scores of radiological trainees, and numerous admiring colleagues. Rigler was also an exemplary husband and father, and the members of his lovely, talented family were devoted to him.

The Minnesota Medical School community also owes a debt of gratitude to Matyl Rigler, his loving, gifted, and supportive wife who over more than five decades appreciated Leo's many accomplishments and contributed to his happiness and peace of mind. Matyl was a charming hostess who helped entertain large numbers of visiting radiological dignitaries. Their engagement to be married, however, had a somewhat inauspicious beginning; Leo was then a junior intern at the Ancker Municipal Hospital in St. Paul where, on evening leave, all interns were obliged to sign in before midnight. The evening Leo and Matyl became engaged, Leo overstayed his visit and missed the 11

o'clock streetcar from Minneapolis and was observed returning to the hospital at 1 a.m. Dr. Ancker, a strict disciplinarian, refused to hear any explanation of the truant's tardiness, and ordered Leo's return to the status of senior medical student or ward clerk. When Dean Lyon heard of Leo's plight, he persuaded Dr. Ancker to reinstate Leo as intern.<sup>5</sup>

In the Annals of the University of Minnesota, Leo Rigler's name will endure as one of its Great Teachers, inspired and inspiring Colleague, and Founder of one of America's finest Schools of Radiology. He has justly earned the Outstanding Achievement Award conferred upon him by Minnesota's Board of Regents in 1960. In all the circles in which Leo Rigler moved he will be sorely missed; his memory will be cherished with great pride and warm affection by all privileged to have known him. His was a life crowned with the diadem and laurels of Victory, worthy of emulation by us all.

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#### We Moved!

The Minnesota Medical Association and MINNESOTA MEDICINE moved into the new Health Association Center on October 9th. The Address is:

Minnesota Medical Association  
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## Anatomical Basis for Retrograde Coronary Vein Perfusion

Venous Anatomy and Veno-Venous Anastomoses  
in the Hearts of Humans and Some Animals

EVE PAKALSKA, M.D.\*† and W. J. KOLFF, M.D. PH.D.\*

Thirty-five human hearts, 36 sheep hearts, 38 pig hearts and 12 dog hearts were injected with Batson's solution or radio-opaque Microfil. Corrosion preparations and X-ray pictures were examined. A clear distinction can be made between large, medium and small veno-venous anastomoses. Large veno-venous anastomoses are mainly located in the apex. Small ones are mainly in the intramuscular plexuses, which anastomose with the thebesian veins. Ischemic areas, which may be expected when the coronary arteries are occluded in 9 different sites are presented and the veins to be used for retrovenous perfusion to avoid the consequences of ischemia are indicated.

Differences were detected in the location of veno-venous anastomoses in different species. Large veno-venous anastomoses seemed to be more prevalent in man. When arterial blood is supplied to a vein with a large anastomosis, much blood may be shunted away instead of being available for retrograde perfusion of an ischemic area.

For diffuse arterial lesions, a retrograde blood supply to ischemic areas can be provided by making an arterial anastomosis or connection with the coronary sinus. Usually the distal part is provided with arterial blood and the sinus is ligated proximally except for a small opening as a safety valve to avoid excessive pressure. The arterialized retrograde blood flow may favor those areas that are starved from blood from the arterial side.

THERE IS A RENEWED interest in arterialization of the coronary veins as a method of surgical treatment of coronary artery disease in cases in which direct revascularization (aorta-coronary bypass) is impossible.<sup>1-5</sup>

Dr. Beck<sup>6,7</sup> began the operation in Cleveland, but he never gained followers in the United States. In Poland, Moll has obtained results in 60 patients (only four deaths) that warrant renewed interest.<sup>3,4,5</sup>† An overview of the history of retrograde coronary vein perfusion, its pros and cons, has been given by Kolff and Kolff.<sup>8</sup> Encouraging experiments with retrovenous perfusion are beginning to appear in increasing numbers.<sup>9-19</sup> A few clinical applications have taken

place in the United States.<sup>1,2</sup> Yet, exact knowledge of the anatomy of the veins of the hearts, their anastomoses and connections is lacking.

We believe that part of the poor results may have depended on perfusion of the wrong vein, or if the right vein was perfused, on shunting of blood away from the ischemic area through a veno-venous anastomosis that was either unrecognized or formed later. Moreover, differences in species have different anatomy of the venous system of the heart. We have undertaken a study of the topographical anatomy of the venous system of the heart, and its anastomoses. We have made comparisons of the hearts of man, sheep, pigs and dogs.

Study of the Thebesian veins and their importance is going on and will be published later.

### Material and Methods

Thirty-five human hearts#, 36 sheep hearts (eight were lambs), 38 pig hearts and 12 dog hearts were used in this study. The human hearts were of adult humans having no detectable cardiovascular disease. The venous vessels and, in a few cases, also the arteries were injected with Batson's solution##, latex-Hycar§

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This work is supported by a grant from the Nora Eccles Harrison Cardio-Vascular Research and Training Institute of the University of Utah (Dr. Abildskov, Director).

†Dr. Pakalska's stay in the United States was made possible through the offices of Dr. Robert Fisher, Director, Office of Europe, Office of International Health, DHEW, Parklawn Building, Room 18-75, 5600 Fishers Lane, Rockville, Maryland 20852.

‡We have data beyond Dr. Moll's last publication through personal communication with Dr. Eve Pakalska.

#The investigations on most of the human hearts have been published earlier, (1970) in Poland.<sup>20</sup>

##Batson's solution — Polysciences Inc., Harrington, Pennsylvania.

§Latex-Hycar — available in Poland.



and yellow radio-opaque Microfil<sup>††</sup>. The injection pressures used were as uniform as possible according to the judgment of the one person (Dr. Eve Pakalska) who performed all the injections. Viscosities of the solutions were accounted for as much as possible. The veins were injected from the right atrium via the coronary sinus, and the anterior cardiac veins via their own individual openings in the atrium. The hearts were corroded in concentrated potassium hydroxide, or in concentrated hydrochloric acid, and the corrosion preparations were inspected with the naked eye and also with a stereoscopic microscope at a magnification of about 20 times. Some of the hearts were injected with radio-opaque material and subsequently x-ray pictures were obtained. In the corroded preparation, the large anastomoses were counted. For the medium anastomoses, representative sections were compared.

### Results

On the basis of our observations, the veno-venous (v-v) anastomoses have been divided according to diameter, into three types: large, medium and small (Figure 1).

<sup>††</sup>Microfil — Canton Bio-Medical Products, Inc., Boulder, Colorado.

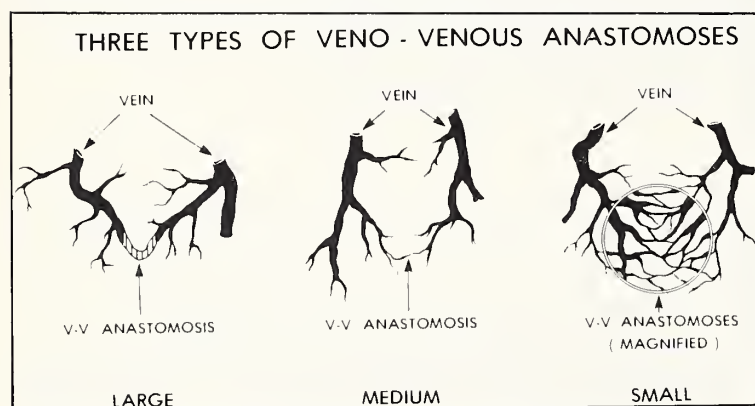


Fig. 1 — Three types of veno-venous anastomoses.

**Large:** v-v anastomoses having a diameter as wide as the diameter of the anastomosing vein in the middle of its course. Diameters of vascular casts measured with an ocular micrometer were larger than 1 mm.

**Medium:** v-v anastomoses having a narrower diameter than the anastomosing vein has in the middle of its course, but it is still visible with the naked eye. Diameters of vascular casts ranged from 500 to 1000 microns.

**Small:** v-v anastomoses visible only at a magnification of about 20 times. Diameters of vascular casts in small v-v anastomoses ranged from 50 to 500 microns.

Large and medium anastomoses are present in the subepicardial course of the cardiac veins. Small anastomoses are present in the intramuscular course of the cardiac veins (Table 1). In studying the topography of the v-v anastomosis, we found that the large v-v anastomoses are in the region of the cardiac apex (Table 2).

Figure 2 shows a sketch of the veins of the heart using the International Nomenclature. (N.A.P., 1956)

Figure 3 describes the most common large v-v

TABLE 1

#### Localization of Veno-Venous Anastomoses

##### Subepicardial

1. apical region (large only)
2. in the course of smaller and larger veins (both large and medium anastomoses)

##### Intramuscular (small only)

1. intramuscular septum and
2. free wall of left ventricle as a multilayered venous plexus
3. free wall right ventricle as a single layered venous plexus

The large and small veno-venous anastomoses are in different locations in the walls of the ventricles.

TABLE 2

#### Groups of Large Veno-Venous Anastomoses in the Region of the Cardiac Apex

Groups of anastomoses		In man	In sheep	In pigs	In dogs
Number of hearts injected:		35	36	38	12
Great cardiac vein to					
I		40%	33%	29%	67%
Middle cardiac vein					
Great cardiac vein to					
Middle cardiac vein and to	II	3%	11%	26%	8%
Left marginal vein					
Great cardiac vein to					
Middle cardiac vein and to	III	27%	5%	25%	17%
Posterior vein of the left ventricle					
Great cardiac vein to					
IV		27%	3%	13%	0
Anterior cardiac veins					

Table 2 discusses only the Large Veno-Venous Anastomoses in the region of the Cardiac Apex. These Large Veno-Venous Anastomoses are important from two points of view:

One, they may shunt away blood from the Myocardium when we try to use veins for retrograde perfusion.

Two, they may act as a safety valve if an artery is directly connected to a vein.



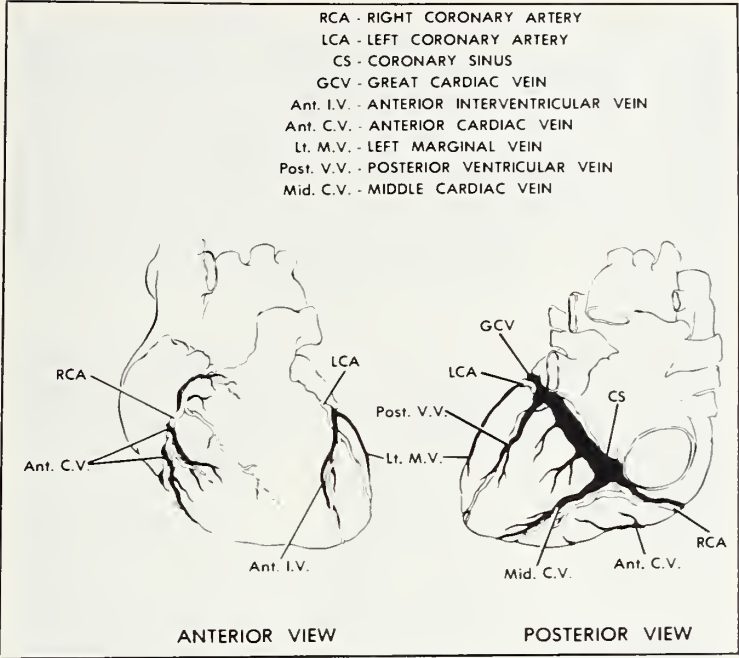


Fig. 2 — Description of abbreviations used in the figures. Internationally agreed terminology, so-called Paris Anatomical Nomenclature. (NAP — 1955)

anastomoses in man, sheep, pigs and dogs observed in the region of the apex.

Table 2 expresses the occurrence of these anastomoses in percent of hearts examined for each species. It is noted that the occurrence of a particular anastomosis varied considerably between species. For example, fewer large v-v anastomoses were seen in the sheep hearts than in man. In eight lamb hearts not listed in that table, no large v-v anastomoses were seen at all.

Medium size v-v anastomoses have been observed in the course of the smaller and bigger veins in the human hearts, as well as in the pig, dog and sheep hearts (Table 3; Figures 4-7). In general, the differences between species here are less than in the large veins.

In the myocardium of the left ventricle and of the intraventricular septum, we have noticed multilayered intramuscular plexus which we have also classified as v-v anastomosis (Figures 8 and 9). In the right ventricle, we have noticed a single layered intramuscular venous plexus.

Discussion

Large sized veno-venous anastomoses in the region of the cardiac apex, previously described by Pakalska<sup>21</sup> in the human and pig hearts, were found in

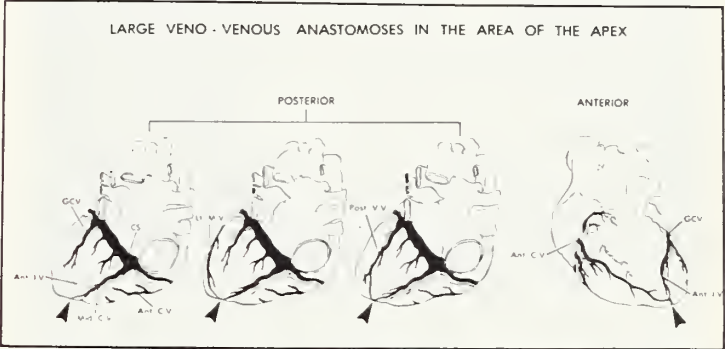


Fig. 3—Large veno-venous anastomoses in the area of the apex. This Figure elucidates Table 2.

TABLE 3  
Occurrence of Medium Veno-Venous Anastomoses.

	Great Cardiac Vein				Position of Anastomoses	Middle Cardiac Vein				Position of Anastomoses
	<u>% of hearts</u>					<u>% of hearts</u>				
	man	sheep	pig	dog		man	sheep	pig	dog	
Middle cardiac vein	27	30	42	17	A, S, VSa, VSp A, VSp VDa	20	10	18	17	VSp, A
Posterior vein of the left ventricle	48	32	30	8		7	0	3	0	A, VDa, VSp
Anterior cardiac veins	53	22	40	40						

Explanations:

- VSa — Ventricular Sinister anterior
- VSp — Ventricular Sinister posterior
- VDa — Ventricular Dexter anterior
- VDp — Ventricular Dexter posterior
- S — Interventricular Septum
- A — Cardiac apex

Great cardiac vein and middle cardiac vein are listed on the top.

Middle cardiac vein, posterior cardiac vein of the left ventricle and anterior cardiac veins are listed on the left side of the Table. (Remember that the anterior cardiac veins are on the right side of the heart)

The Table lists the recurrence of medium size veno-venous anastomoses in percentage of hearts counted for each species. There are substantial differences.

In the diagram of Figure 1 only one medium sized veno-venous anastomoses is drawn. Actually, there are many and their importance lies in the fact that they may increase in size.



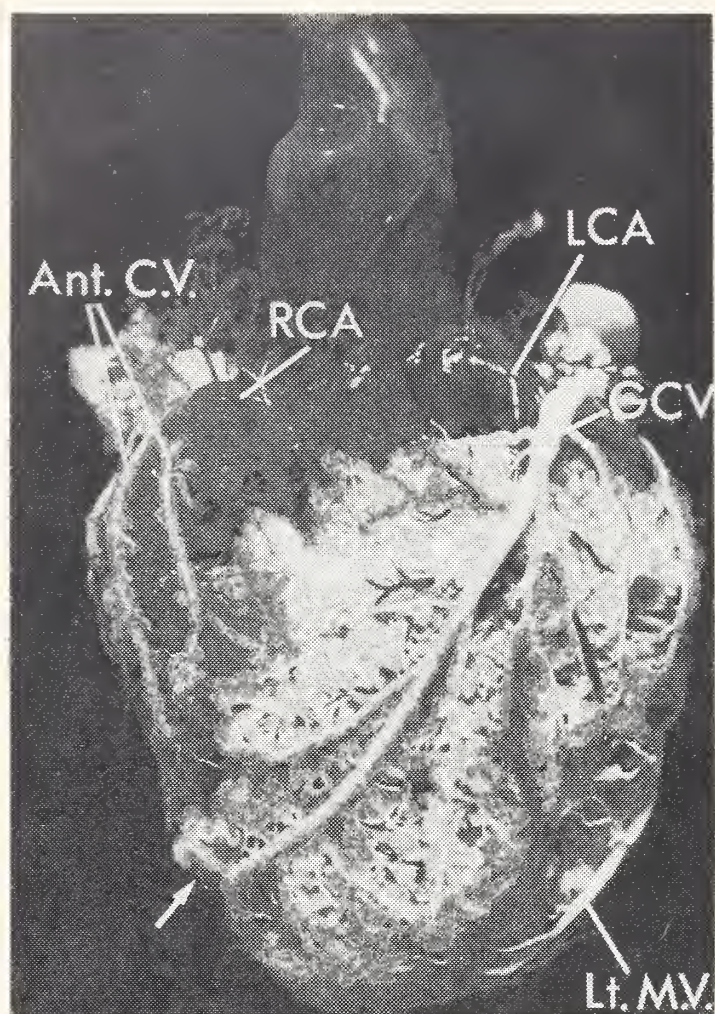


Fig. 4 — Corrosion preparation of the coronary blood vessels (arteries — dark; veins — light) in sheep, injected with Batson's solution (frontal view). V-v anastomoses marked with arrows.

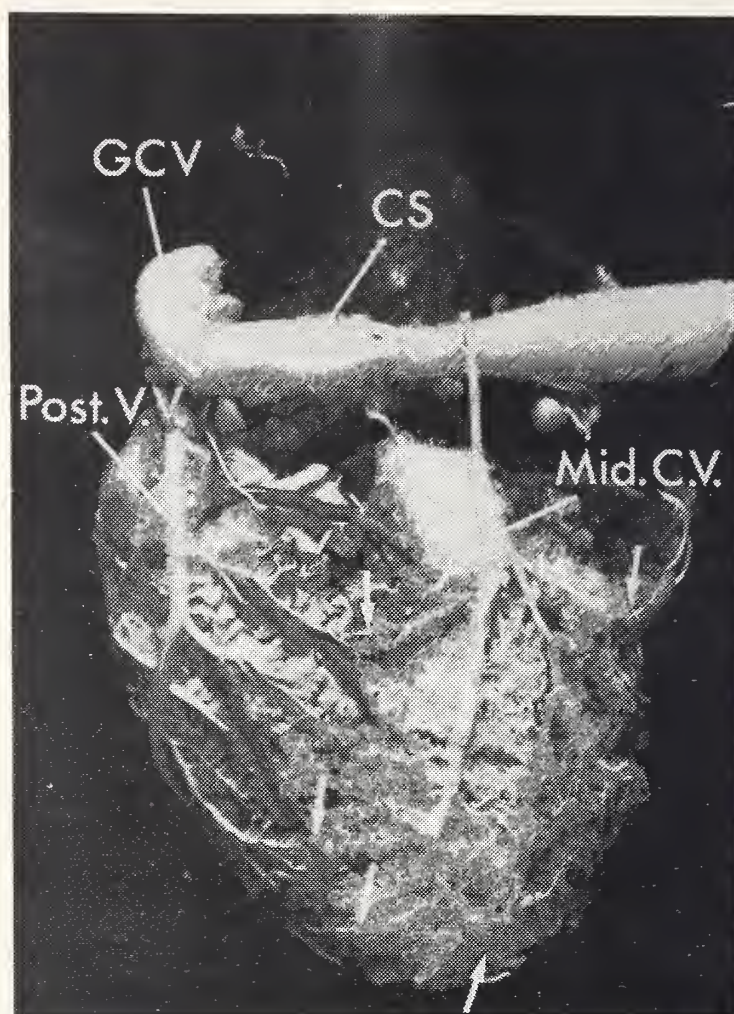


Fig. 5 — Corrosion preparation of the coronary blood vessels (arteries — dark, veins — light) in sheep, injected with Batson's solution (back view).

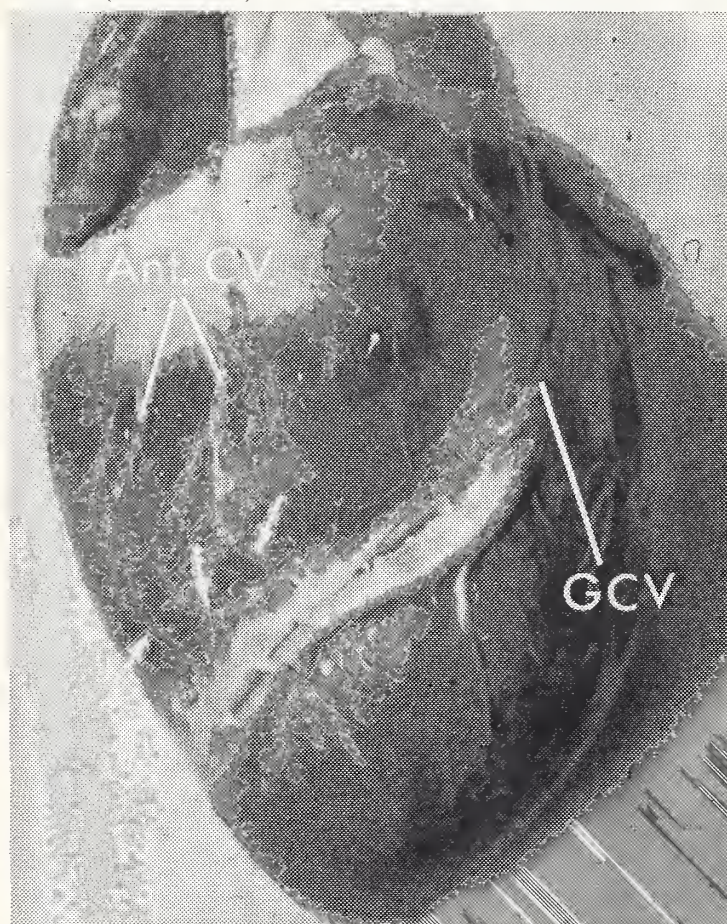


Fig. 6 — Costosternal surface of the pig heart. Cardiac veins filled with Batson's solution. Visible large v-v anastomoses connect anterior cardiac veins with great cardiac vein.

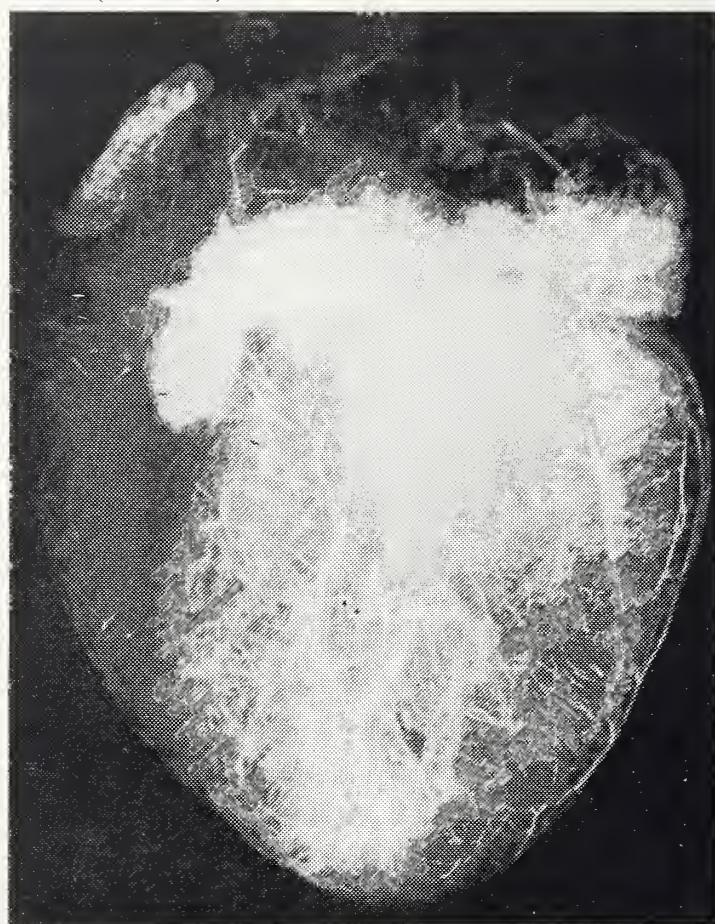


Fig. 7 — Angiogram of the cardiac veins filled with radio-opaque Microfil. Visible v-v anastomoses (large and medium).



97% of the human hearts, in 93% of the pig hearts and in 96% of the dog hearts. Fewer (49%) anastomoses of this type were present in the sheep hearts and there were no anastomoses in lamb hearts. This discrepancy between mature sheep and lambs is in agreement with the view that the number of v-v anastomoses increase with age.

Parsonnet<sup>22</sup> described two constant venous anastomotic rings in human hearts. The first connects the beginning of the middle and great cardiac veins. He found this in 90% of the observed hearts. We found this type of veno-venous anastomoses in 40% of the human hearts. A second venous anastomotic ring was also described by Parsonnet<sup>22</sup> and was found in 70% of all human hearts. It connected the posterior vein of the left ventricle, middle cardiac vein and left marginal vein. We have not found this v-v anastomosis in our animal hearts.

In normal hearts, the most important veno-venous anastomoses from the standpoint of possible surgery are those: (a) between the great cardiac (which empties via the coronary sinus into the right atrium) and the anterior cardiac veins (which have isolated openings into the right atrium) and (b) the veno-venous anastomoses between the great and middle cardiac

vein. This latter vein has an opening in the distal part of the coronary sinus in the human heart, but sometimes empties directly into the right atrium close to the coronary sinus in the animal hearts. We noticed that in the human heart, more large v-v anastomoses connect the anterior cardiac veins with the great cardiac vein than in animals (Table 2). These anastomotic pathways may be important in attempts to revascularize the ischemic heart by arterialization of the coronary sinus. These anastomoses may act as safety valves to release unduly high pressure in the sinus. The absence of them may explain the occurrence of a cardiac edema in sheep when the arterialization of the sinus is undertaken in this species.

The medium and small veno-venous anastomoses were found in the myocardium and on the epicardial surface of the heart. Although some studies<sup>21,23</sup> have mentioned that smaller veno-venous anastomoses exist in the heart, no quantitative data on these types of anastomoses have previously been published.

Supported by the concept that the number of veins in the heart increases with age,<sup>24,25</sup> we believe that the

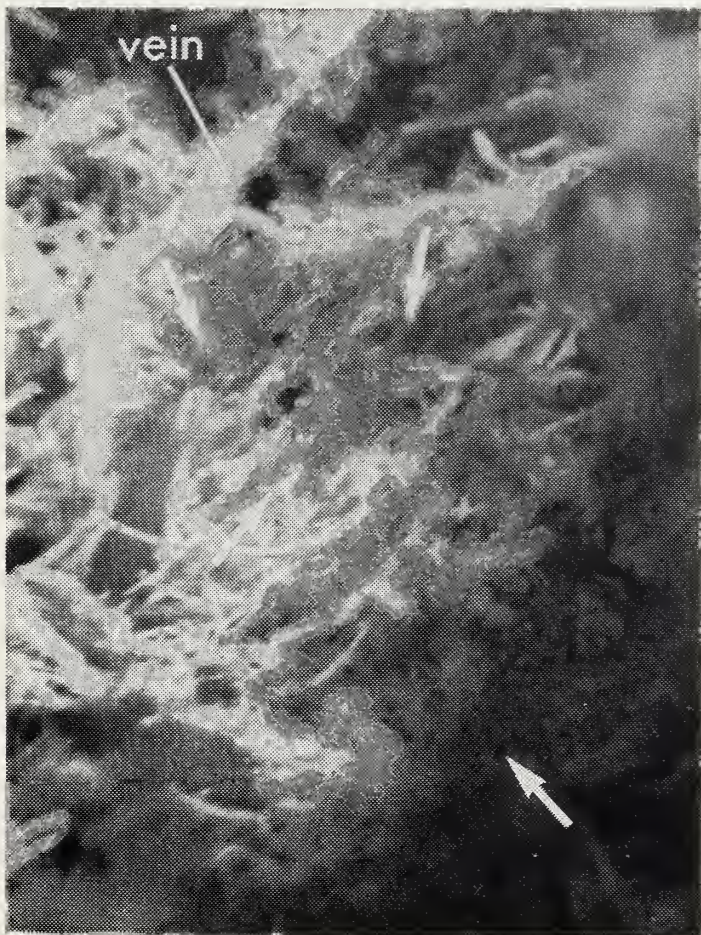


Fig. 8 — Corrosion preparation of the veins of the interventricular septum filled with Batson's solution. Visible multilayered intermuscular venous plexus (small v-v anastomoses). Magnification about 50 x.



Fig. 9 — Corrosion preparation of the veins of the anterior wall of the left ventricle (filled with Batson's solution). Visible multilayered intermuscular venous plexus (small v-v anastomoses). Magnification about 25 x.



veno-venous anastomoses form a potential route for the blood to return from the myocardium to the heart chambers.

Veno-venous anastomoses may or may not be advantageous during retrograde perfusion. If the anastomoses are fully dilated they may shunt the blood directly into the right atrium.<sup>22</sup> Not enough pressure head would remain in the vein to provide retrograde perfusion of the myocardium. On the other hand, some veno-venous anastomoses may be a safeguard against high pressures and may prevent the formation of hemorrhages in the left ventricle, which is sometimes seen in the animal experiments, but so far has not been seen after retrograde perfusion of human ischemic hearts, not even in the growing experience of Moll.\*

We have observed more v-v anastomoses in human hearts than in any of the animals we investigated (especially sheep). For this reason, arterialization of the distal† half of the coronary sinus, which has been successfully performed on human patients (Moll<sup>3</sup>) may cause acute edema in healthy animals because of the lack of enough veno-venous anastomoses to alleviate

\*Personal communication from Dr. Moll to Dr. Eve Pakalska.

†“Distal half” of the coronary sinus we call the half that normally derives its blood from the small veins in the heart, “proximal” is the half that has the orifice in the right atrium.

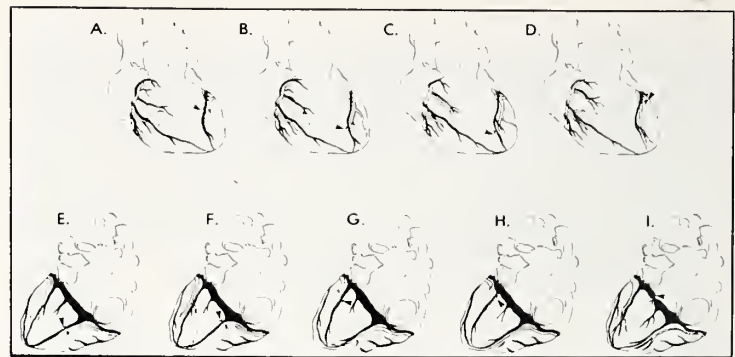


Fig. 10 — Various localizations of the ischemia and possibilities of using the regional vein for the retrograde perfusion. Sites of an ischemia are listed and the location of the coronary artery occlusion that usually causes it is given. The veins that normally drain the area and that may be used to provide the area retrograde with arterial blood are indicated with arrows. Possibility of blood outflow through large veno-venous anastomoses is also indicated, and the names of the veins are listed in Table 4.

- A. Antero-lateral ischemia — disease of the distal LAD.
- B. Antero-septal ischemia — disease of the right branch of LAD.
- C. Apical ischemia — disease of the terminal portion of LAD.
- D. Antero-basal ischemia — disease of the circumflex branch of LCA.
- E. Postero-inferior ischemia — disease of the posterior interventricular branch of LCA.
- G. Postero-lateral ischemia — disease of the circumflex branch of LCA.
- H. Postero-basal ischemia — disease of the proximal part of circumflex branch of LCA.
- I. Diffuse ischemia — multivessel disease.

TABLE 4

**Description of Ischemia Located in Different Areas, Veins for Perfusion and Possible Anastomoses.**

Localization of ischemia	Coronary arterial obstructions leading to infarct	Choice of vein for retrovenous perfusion	Possibility of outflow through v-v anastomoses of the large type
antero-lateral-figure A	anterior interventricular branch of left coronary artery	anterior interventricular vein	middle cardiac vein, posterior ventricular vein & anterior cardiac veins
antero-septal-figure B	right division of anterior interventricular branch of left coronary artery	anterior interventricular vein	middle cardiac vein, posterior ventricular vein & anterior cardiac veins
apical-figure C	terminal portion of anterior interventricular branch of left coronary artery	anterior interventricular vein in the beginning of its course	middle cardiac vein, posterior ventricular vein & anterior cardiac veins
antero-basal-figure D	*/circumflex branch of left coronary artery	left marginal vein or great cardiac vein on the left margin of heart	middle cardiac vein, posterior ventricular vein & anterior cardiac veins
postero-inferior-figure E	posterior interventricular branch of right coronary artery	middle cardiac vein ½ part of its course	great cardiac vein, posterior ventricular vein
postero-septal-figure F	right coronary artery or its posterior interventricular branch	middle cardiac vein	great cardiac vein, posterior ventricular vein
postero-lateral-figure G	*/circumflex branch of left coronary artery	posterior ventricular vein/left/	middle cardiac vein, great cardiac vein
postero-basal-figure H	*/circumflex branch of left coronary artery	posterior ventricular vein/left/	middle cardiac vein, great cardiac vein
diffuse ischemia multivessel disease figure I	disseminated extensive narrowing of several arteries	½ of coronary sinus	middle cardiac vein, anterior cardiac vein, posterior ventricular vein

\*/variations in vessels distribution

Table 4 offers nine possibilities for possible locations for arterial obstruction which may lead to infarction, the lowest row includes disseminated or diffuse changes in the arteries, which may lead to ischemic damage anywhere. Compare Figure 10.



excessive pressure. (Moll presently also leaves a small opening as a safety valve; he does not tie the sinus off completely any more, as he has done in the past).

There is a great deal of controversy about the possible benefit of retrograde perfusion of the coronary vein or veins with arterial blood. Obviously, if one perfuses a vein that does not correspond to the ischemic area or if a wide anastomosis shunts the blood back into the atrium, no benefit will be derived. We believe that the appropriate vein used for perfusion should be determined according to the localization of the occlusion in each case. For this reason, we have indicated in Figure 10 which veins should be arterialized for the most common infarcts. Table 4 presents the data in table form. The lowest lines of Table 4 indicate that in case of disseminated or widespread atherosclerosis of the coronary arteries on the left side, one may use the distal half of the coronary sinus as is presently done by Moll with considerable clinical success.

Only one single anastomosis to the coronary sinus is required to retroperfuse most of the myocardium. Individual anastomoses to all the veins accompanying the diseased arteries are not required since there are no functional valves in the coronary veins. One anastomosis with the distal half of the coronary sinus would suffice to reach its entire stream bed. However, as long as the effective lifespan of retrograde perfusion is not known, one wants to interfere as little as possible, for non-diffuse disease retroperfusion of an individual vein should be considered. Then not only will the surgeon have to learn the topographical anatomy of the coronary veins, but also he will have to

know the most frequent occurrence of veno-venous anastomoses. They have been listed in Table 4 and have been indicated in Figure 10. Fortunately, the veins are never arteriosclerotic to begin with.

Where does the blood go if we perfuse the coronary veins retrograde when it does not shunt via v-v anastomoses? The answer to this question is presently under study. We suggest that most of it returns via the intramuscular venous plexus and via the sinusoids to the Thebesian veins.

What about gas exchange and nutrition? The plexus but particularly the sinusoids have very thin walls. They surround the myocardial fibers and anastomose with capillaries. In all three: plexus, sinusoids and capillaries, gas exchange and nutrition can take place.

What is the long range fate of the arterialized coronary veins? Do they become sclerotic? In the earlier experience of Beck<sup>6</sup> in dogs' veins, sclerosis took place, according to personal communication from Beck's former associate Feininger. Their dogs did not die, however, although their coronary arteries had been tied off.

For human patients needing retrograde perfusion of the veins, we do not know what the fate of these veins will be. Retrograde perfusion of the coronary vein by surgery is indicated only in desperate cases where all other attempts have either failed or are deemed to be inappropriate. It is hoped that acute relief of ischemia can be obtained by retrograde perfusion of the coronary sinus or part of it by cardiac catheter. This might tide a myocardium (and a patient) over until this patient can be taken to the operating room for more definitive help.

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# Minnesota Department of Health

## Cancer Rates in a Community Exposed to Low Levels of Creosote Components in Municipal Water

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IN NOVEMBER, 1978, the Minnesota Department of Health detected minute (nanogram per liter) quantities of various polynuclear aromatic hydrocarbons (PAH), including pyrene, fluoranthene, anthracene, and naphthacene, in several municipal and industrial wells in the city of St. Louis Park, a suburb of Minneapolis<sup>1</sup>. Although there are no official U.S. standards for PAH in water supplies, four municipal wells were closed immediately because the amounts exceeded the World Health Organization's recommendation for safe levels in drinking water<sup>2</sup>. PAH compounds were not detected in the remaining ten municipal wells.

The PAH compounds apparently originated from the site of a plant which distilled coal-tar products and treated wood with creosote from 1917 to 1972. During this time, wastes from the plant's operations were deposited on the surface of the site, allowing contamination of the groundwater reservoirs below.

It is not known how long PAH compounds have been in the St. Louis Park water supply, since techniques for their detection in water have only been available in the past few years<sup>3</sup>. A well drilled in 1932, however, was shut down within a few months due to a creosote-like odor and taste of the water, and it is possible that PAH compounds have been in the municipal water for many years or decades in low concentrations.

The occurrence of PAH in the environment is of concern because of their demonstrated carcinogenicity for animals and/or mutagenicity for bacteria.<sup>4,9</sup> There appear to be no epidemiologic studies of human populations exposed to low levels of PAH in water supplies, although the association of occupational skin cancer with creosote and coal-tar compounds has long been known<sup>10,13</sup>.

The Minneapolis-St. Paul area, including St. Louis

Park, was part of the Third National Cancer Survey<sup>14</sup> conducted for the three years, 1969 to 1971. All hospital records in the five county Twin Cities area were searched for cancer diagnoses, and abstracts of cancer records were coded on computer tape. Because of the availability of these records on tape, albeit for a limited three year period of time, it was decided to compare cancer incidence rates in St. Louis Park with those in the nearby municipalities of Edina and Richfield and in the entire Minneapolis-St. Paul Standard Metropolitan Statistical Area (SMSA).

### Methods

Incidence rates for 45 types or sites of cancer were calculated for St. Louis Park, Edina, Richfield, and the Minneapolis-St. Paul SMSA using data from the Third National Cancer Survey for the three years, 1969-1971. Richfield was selected because it was a SMSA suburb similar to St. Louis Park in social and economic characteristics such as median school years completed, percent high school graduates, occupation and median and mean family income. Edina was selected because the creosote contamination was believed, at that time, to be moving toward Edina. The entire SMSA was used as the major comparison area. Incidence rates were age-adjusted to the SMSA populations of white males and white females respectively. Calculations were done of average annual age- and sex-specific cancer incidence rates, age-adjusted incidence rates, standard incidence ratios (SIR), Mantel-Haenszel overall summary Chi-squares<sup>15,16</sup> and Z statistics. The latter two statistics are used to assess the significance of the difference between two rates after adjusting for age. Population denominator data were taken from the 1970 U.S. Census<sup>17</sup>.

### Results

For males, no cancer rates in St. Louis Park were statistically significantly different from those in the three comparison areas. Among females, age-adjusted rates for all cancer sites combined, for breast cancer, and for cancers of the gastrointestinal tract were higher

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in St. Louis Park than in Edina, Richfield, and the SMSA. The excess in gastrointestinal cancer rates for females was only slightly significant ( $P < .05$ ) but all cancer sites combined and breast cancer had differences with a high degree of statistical significance ( $P < .0005$ ). Further details of the significant comparisons are given in the Table.

### Discussion

In the absence of epidemiologic literature on ingested exposure to PAH, it is of interest to note that rats fed one PAH compound — 3-methylcholanthrene — develop mammary carcinoma in high frequency and these tumors occur almost exclusively in females.<sup>18-20</sup> Other PAH compounds produce a variety of tumors in animals<sup>4</sup>.

Breast cancer rates vary considerably with geographic location and with characteristics of the population<sup>21,24</sup>. In the Third National Cancer Survey<sup>14</sup>, for example, the rates varied from 59 to 83 per 100,000 white females per year in the nine different study areas. In a recent review of the epidemiology of human breast cancer, Kelsey has summarized the influence of major factors known to influence breast cancer rates, expressing the results as relative risks (RR) — the ratio of case rates in a population with the factor to the rate in those without the factor<sup>24</sup>. These include: (1) First degree relative with breast cancer (RR of 2-4); (2) Absence of or late age at first full-term pregnancy (RR of 2-4); (3) History of fibrocystic disease of the breast (RR of 2-4); (4) Exposure to high levels of radiation to the chest (RR of 2-4); (5) Upper socio-economic class (RR of 2-4); (6) Obesity (RR of 2-4); and (7) Early age at menarche and late age at

menopause (RR of 1.1-1.9). Rates given in the literature for Jewish populations are contradictory, varying from less than to higher than those for non-Jewish whites<sup>25,27</sup>. The contribution of these factors to the difference in breast cancer rates between St. Louis Park and the comparison areas cannot be evaluated without further information about the individual cases. Because of the sizable population with Jewish ancestry, estimated to be 20% in 1971<sup>28</sup>, the influence of this factor is of particular interest, but would not explain the 1.5 fold difference in rates even if 20% of the St. Louis Park breast cancer cases were Jewish and a two-fold relative risk existed.

The lack of elevation in the rates for the great majority of cancer types is reassuring, but factors responsible for the elevation in breast cancer rates in St. Louis Park need to be investigated. Further interpretation must await interviews of the 95 cases of breast cancer or their families and an appropriate control group. The results of such a detailed case-control study, now in the planning phases, may explain the elevated breast cancer rates in St. Louis Park on the basis of the frequencies of known risk factors. If this is not the case, further studies to explore a possible relationship with the water supply must be considered.

At the present time, the elevated incidence of breast cancer cannot be attributed to the water contamination, although the limited information available does not rule out such an association. It should be noted that the wells found to be contaminated have been closed, presumably reducing any hazard which may have been present.

TABLE  
Cancer Incidence Rates for Total Cancers and Breast Cancer  
St. Louis Park and  
Three Comparison Populations  
White Females Only, 1969 to 1971

	Breast Cancer			All Cancers	
	Population	Total Cases 1969-1971	Average Annual Age-Adjusted Rate* per 100,000 pop.	Total Cases	Average Annual Age-Adjusted Rate* per 100,000 pop.
St. Louis Park	25,424	95	113	301	381
Edina	22,492	65	82	175	241
Richfield	24,247	41	58	145	235
MSP SMSA	914,218	2130	78	7726	282

\*Rates per 100,000 white females, adjusted to the MSP SMSA population of white females, 1970.

#### Mantel-Haenszel Summary Chi-Square Values and $P$ -Values

Comparison	CHI-SQUARE		$P$ -VALUE	
	Breast Cancer	All Cancers Females	Breast Cancer	All Cancers Females
St. Louis Park vs Edina	3.38	19.90	.05 < $p$ < .1	< .0005
St. Louis Park vs Richfield	10.85	21.18	.001	< .0005
St. Louis Park vs SMSA	13.64	24.31	< .0005	< .0005



#### Acknowledgment

We gratefully acknowledge the advice and assistance of Marcus Kjelsberg, Ph.D., Chairman, Division of Biometry and of Leonard Schuman, M.D., M.S., Chairman, and Jack Mandel, M.P.H., Assistant Director, Division of Epidemiology, University of

Minnesota School of Public Health, Minneapolis, Minnesota. Dr. Schuman was Director of the Minneapolis-St. Paul Component of the Third National Cancer Survey, and kindly provided access to the data.

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### MMA Annual Meeting, May 20-22, 1981

#### "Common Medical Experiences"

#### Radisson South Hotel, Bloomington

"Common Medical Experiences" is the theme selected by the Subcommittee on Scientific Assembly for this year's scientific program. Physicians from all parts of the state, representing multiple specialties, will convene in Minneapolis May 20-22, 1981; mark your calendars now.

Participants in the scientific program will explore from various viewpoints problems and experiences which are common to diverse groups of physicians. Over 25 courses will cover topics with wide appeal. Presentations will be made by a multispecialty faculty representing various institutions and locations in the state. There will be ample time for audience-faculty interaction.

Among the many opportunities offered at the MMA Annual Meeting are fellowship with colleagues, discussions of clinical concerns and consideration of issues facing organized medicine.

Watch for further information in future issues.

Questions? Contact: Department of CME & Program Services

Minnesota Medical Association

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#### Cover Photograph

#### "Winter's North Shore"

Dr. Earl C. Henrikson takes an annual trip to the North Shore with the Minneapolis Chapter of the Audubon Society. The members of the Society check the winter birds as well as the boundaries of the lake shore, trails, and streams. It was during one of these trips that the cover photograph was taken.

Dr. Henrikson is a Minneapolis surgeon and has been a yearly contributor to the covers of MINNESOTA MEDICINE. His cover "Waiting for Breakfast" (November, 1978 issue of MINNESOTA MEDICINE) won the Outstanding Cover Award.



# Fracture Conference

## Lateral Ligament Injuries of the Ankle

JAN P. DeROOS, M.D.\*; BRIAN T. BRIGGS, M.D.\* and KENNETH A. JOHNSON, M.D.†

**Dr. Kenneth A. Johnson:** Lateral ligamentous injuries of the ankle are extremely common and most of us have incurred one of these injuries at some time to some degree. The term "ankle sprain" for these lateral ligamentous ankle injuries is as nonspecific as "broken leg." We hope to show how these lesions can be defined more accurately and given rational treatment.

**Dr. Jan P. DeRoos:** A 28-year-old railroad worker had a severe "sprain" of the right ankle while playing high school football. At the time of injury, no cast immobilization or adhesive strapping was used; the patient was merely given an Ace bandage. Over several weeks, he gradually resumed his activities. During the next 10 years he had multiple "sprains" and a chronic discomfort in the ankle. He now works

for the railroad and his job requires him to walk on and over railroad ties. He finds that inversion stress put on his ankle by his work produces significant pain.

**Dr. Johnson:** The routine roentgenograms were thought to be negative (Figure 1). Doctor Barron, would you like to see any other views?

**Dr. Stephen E. Barron:** Yes, I would like to see lateral as well as anterior stress views of both ankles.

**Dr. Johnson:** Here are the stress views of both ankles (Figure 2). You can see that he has 7° of talar tilt on the left ankle with inversion stress while the foot is in about 60° of plantar flexion, and 32° on the right. Would you say that that was a significant talar tilt?

**Dr. Barron:** Yes, I would. It is reported<sup>1</sup> that ligament rupture is probably present if the amount of inversion tilt of the talus on the affected side is 6° (or more) greater than on the healthy side.

**Dr. Mark B. Coventry:** Incidentally, while you are looking at the lateral views, I think that it would be well

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†Consultant, Department of Orthopedics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Reprint address: Dr. K. A. Johnson, Mayo Clinic, Rochester, MN 55901.

Fracture Conference, May 5, 1976.



Fig. 1 — Anteroposterior (*left*) and lateral (*right*) views of right ankle in Case 1.



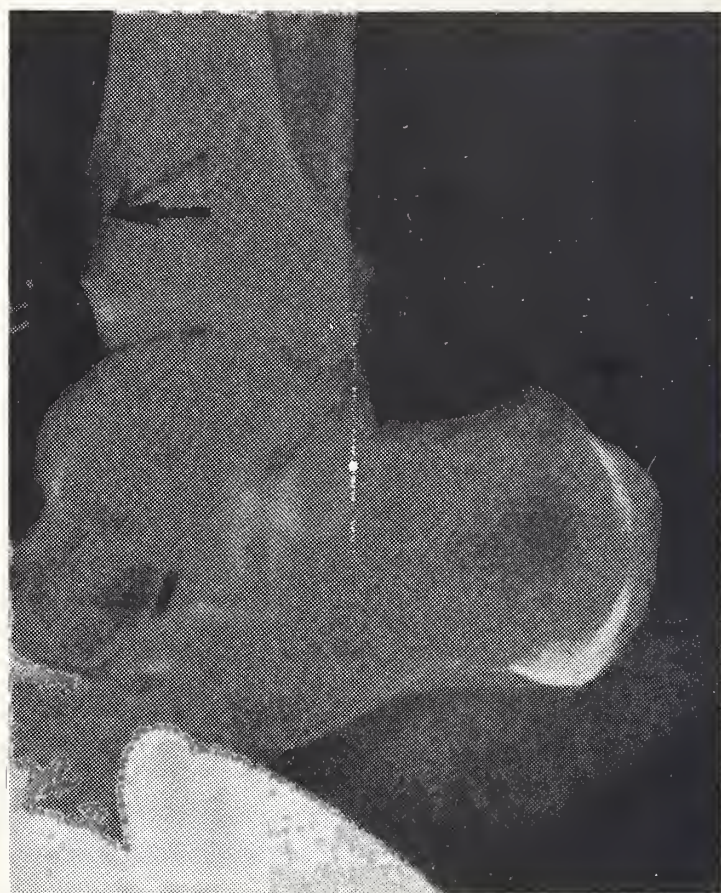
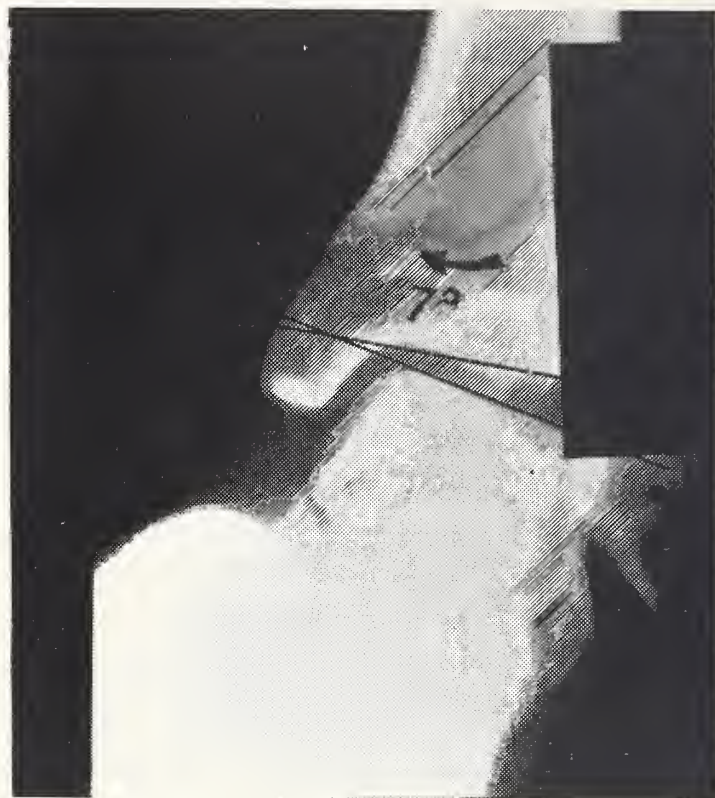


Fig. 2 — Inversion stress views demonstrating increased talar tilting of right ankle (*upper left*) compared with left ankle (*upper right*). Anterior stress views showing incongruence of dome of talus with distal tibia articular surface on right ankle (*lower left*), compared with left ankle (*lower right*).



for everyone to be alert to recognize a calcaneonavicular bar in a patient. This is not present here, but I have seen some "sprains" treated for a long period when, in fact, the patients had unrecognized tarsal coalitions.

**Dr. Johnson:** Evaluating the anterior stress views (Figure 2 *lower left* and *lower right*), we can see that the right ankle shows a subluxation of the talus anteriorly on the tibia. One should focus on the congruence of the dome of the talus and distal tibia with the stress applied to the posterior calcaneus. Incidentally, in these patients with chronic ankle problems, these stress views can be obtained without any anesthesia, which often is required at the time of acute injury.

An arthrogram was also done (Figure 3) and demonstrated extravasation of dye into tendons behind both the medial and lateral malleoli. The dye leakage into the peroneal tendons is known to be a finding in some arthrograms of normal ankles,<sup>2</sup> although it usually represents a tear of the calcaneofibular ligament. The leakage of dye into the flexor hallucis and flexor digitorum tendons is less well known. Broström et al.<sup>3</sup> have reported that 25% of normal individuals have this finding on ankle arthrograms. No contrast material leaked anteriorly through the anterior lateral capsular region.

Doctor Barron, in view of the patient's history and the findings, would you recommend surgical treatment for this patient's ankle problems?

**Dr. Barron:** Yes, I believe he has enough instability and resulting disability to justify reconstruction of the ankle ligaments.

**Dr. Johnson:** This was done and a satisfactory result obtained. Doctor Henderson, would you comment on the results of late reconstruction of lateral ankle ligaments?

**Dr. Edward D. Henderson:** From my experience and from the cases reported,<sup>4</sup> the results are very good after late reconstruction of lateral ankle ligament instability. This is in contradistinction to the knee in which late repair is technically demanding and unpredictable.

**Dr. DeRoos:** Our second case is that of an acute lateral ligamentous injury rather than of a chronic problem. The patient, a good high school basketball player, severely inverted his right ankle in practice. He was seen initially by his personal physician who saw no fractures on roentgenograms but who was concerned because of massive swelling on the lateral aspect of the ankle. The patient was referred to this institution, where we saw him about 24 hours after the injury. The



Fig. 3 — Arthrogram showing contrast material extravasated into medial flexor tendons as well as into lateral peroneal tendons.

ankle was ecchymotic, swollen, and quite painful with any motion.

**Dr. Johnson:** The routine roentgenograms appeared to be normal (Figure 4). He was a vigorous young man with aspirations of playing college basketball. Stress roentgenograms were performed with the patient under general anesthesia (Figure 5).

What do you think of these stress views, Doctor Braun, and would you have a suggestion as to treatment?

**Dr. Donald P. Braun:** He has a significant talar tilt on the inversion views of his right ankle. I believe that the best way to treat him would be cast immobilization for three to four weeks. If he has significant residual instability, then one could always do a late reconstruction, as suggested by Laros.<sup>5</sup>

**Dr. Johnson:** Doctor Braun is one who would apparently not operate on complete acute ankle ligamentous tears. I think, however, that there is an increasing awareness that operative intervention is



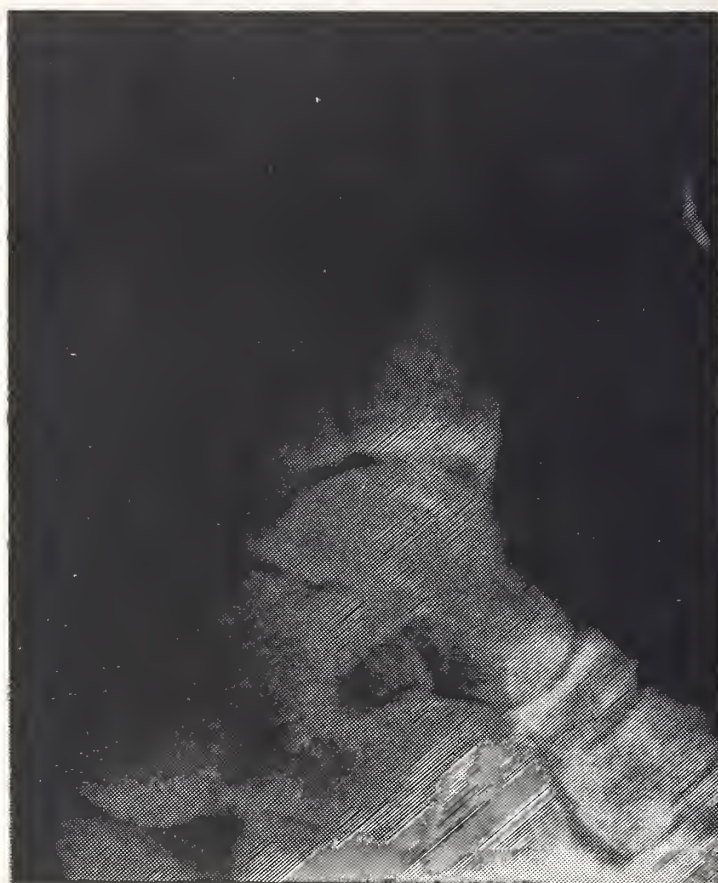


Fig. 4 — Anteroposterior (*left*) and lateral (*right*) views of right ankle in Case 2.

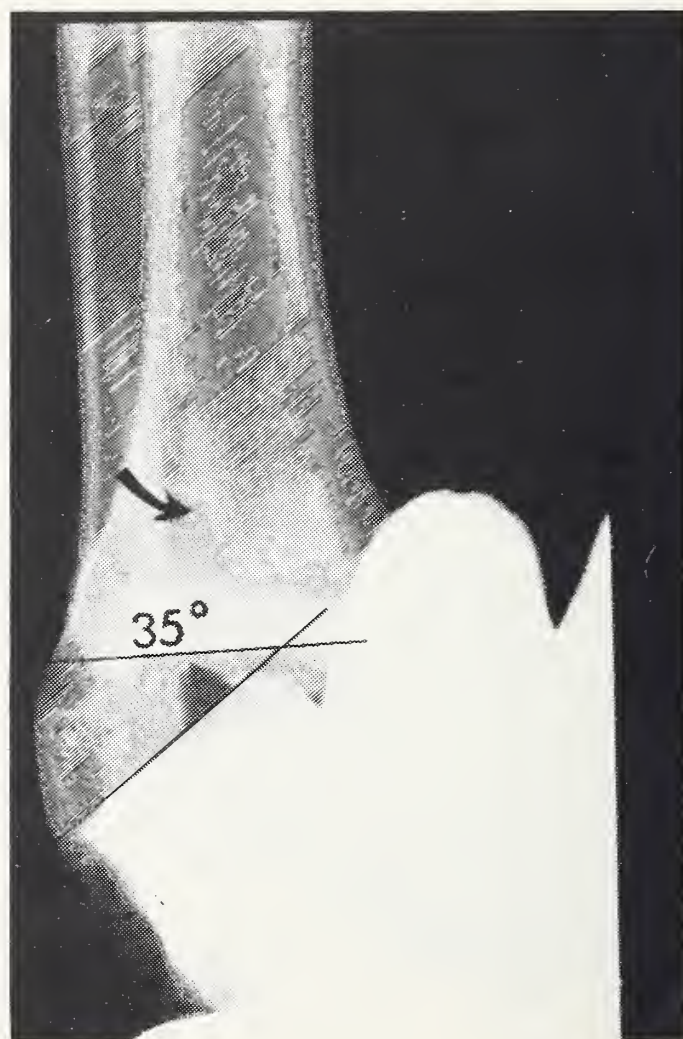
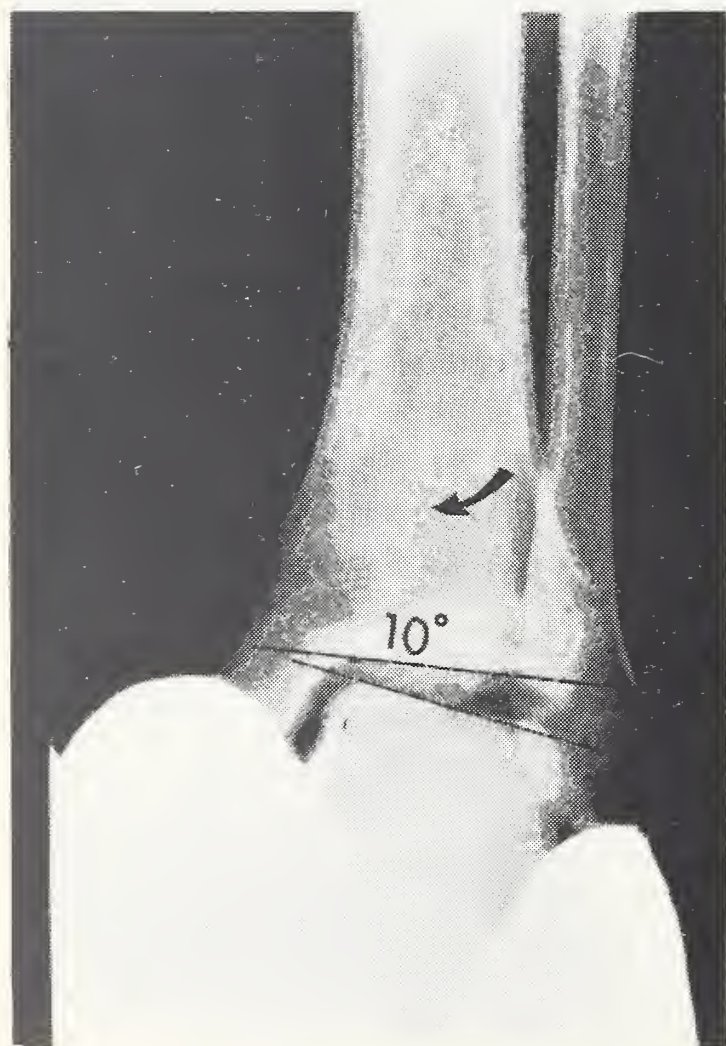


Fig. 5 — Inversion stress views show increased talar tilting of right ankle (*right*) compared with left ankle (*left*).



indicated in some cases. We know that this young man has significant instability with this acute injury. We also must realize that he is not just an average athlete. He desires to continue his athletic career on a higher level of competition and he appears to have the ability to do so. From what we have read in the recent literature,<sup>1,6-11</sup> surgical repair of acute ligamentous ruptures is the only way to guarantee a superior athlete the completely stable ankle that he requires. We believed that we could best offer this young man a stable ankle with a high degree of certainty by doing surgical repair of the ligaments. However, the hazards of surgical repair — such as infection and anesthetic risk as well as a period of hospitalization — certainly need to be weighed against the advantages of a stable ankle.

**Dr. Henderson:** Doctor Braun mentioned cast immobilization as his form of treatment. In my opinion cast immobilization is unnecessary in the treatment of lateral ankle ligament injuries. It unnecessarily adds muscle atrophy and weakness to the situation. I believe one should treat the severe injuries either with operative repair of the ligaments or with adhesive strapping and protected mobilization.

**Dr. Johnson:** This patient had an operative repair of his ligamentous rupture. A complete tear of the anterolateral ankle capsule and anterior fibulotalar ligament was found (Figure 6.)

**Dr. Coventry:** I think that there is a considerable parallel between injuries to the ligaments of the ankle and of the knee. It took orthopedic surgeons a long time to accept the concept of early operative repair of acute ligamentous knee injuries. We now accept it readily. Now we are questioning the necessity of the early operative repair of the ankle injuries — I think that the historical parallel between the ankle and the knee is very clear and instructive.

**Dr. DeRoos:** We will try to summarize this conference briefly by outlining what we feel is the rational treatment of an ankle "sprain." One has to evaluate critically the history of the ankle injury and do a careful physical examination. This is the first step in a rational treatment program. And this critical first step is vital if the physician is to begin to screen out those patients who have the more significant complete ligamentous

ruptures from those who have the less significant incomplete ligamentous strains. A complete rupture often occurs in heavy athletic competition and is usually accompanied by severe pain, immediate swelling, audible tearing of the ligaments, and gross ecchymosis about the heel and both sides of the ankle. The less significant injury may allow weight bearing for along time before pain becomes significant and usually shows some improvement in five to seven days.

The minor injury appears to be best treated with serial adhesive ankle strappings and mobilization. If a major ligamentous rupture is suspected, roentgenographic stress views are then indicated. The patient one might consider for operative repair would be the young athletic person needing a stable ankle for work or strenuous activity. Stress views under local, regional, or general anesthesia can usually permit the physician to differentiate the unstable from the stable ankle joint. Arthrography is indicated in those situations in which there is some question of the extent of injury after the stress views are taken.



Fig. 6 — Operative view showing sutures through torn anterior fibulotalar ligament and ankle capsule. Forceps are holding stretched but not completely ruptured fibulocalcaneal ligament.

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- 9-11. Will be found on page 778



# Minnesota Medical Association

*from*

## *Division of Socio-Economic Affairs*

James H. Sova, Assistant Executive Vice President

Lynn R. Gruber, Director, Department of Medical Services and Research

George C. Lohmer, Jr., Director, Department of Health Planning

Charles W. Wiger, Director, Department of Legislative Affairs

### **Department of Medical Services and Research**

In 1976 the Minnesota Legislature passed a series of laws on the regulation of certain occupations. The intent of the legislature was to ensure that no regulation would henceforth be imposed upon any occupation unless required for the safety and well being of the citizens of the state. Minnesota Statute 214.13 declares that "the Commissioner of Health shall promote the recognition of human services occupations useful in the effective delivery of human services." This law empowers the Minnesota Commissioner of Health to establish procedures for the identification of human services occupations not currently credentialed by the state. Through the work of a Human Services Occupations Advisory Council (HSOAC) the Commissioner is aided in determining the appropriate regulatory model, if any, for the applicant groups. Such regulatory modes include: extension of common law, statutory causes of civil action, inspection requirements and enforcement power, registration and licensure.

Within the past few years a number of unregulated human service occupation groups have filed applications with the HSOAC body for a determination of appropriate credentialing. These groups include: athletic trainers, chemical dependency counselors, contact lens technicians, physicians assistants, social workers, paramedics, x-ray technicians, speech pathologists/audiologists and acupuncturists.

The process for achieving a classification of regulation, if it is needed, is a slow and sometimes complex process. The HSOAC initially reviews new applications, assigns a small subcommittee to initiate as many meetings as are necessary to learn about and question the applicant group and then requires the subcommittee to present its recommendations and rationale to the full HSOAC who in turn discusses the applicant group in light of the subcommittee's recommendation. Finally, HSOAC makes a formal, written recommendation to the Minnesota Commissioner of Health for his consideration.

Complexity arises when a group such as the lay acupuncturists makes an application for credentialing. The HSOAC feels obligated to review the application in the normal committee fashion due to the charge stated in the statute and due to the desire of the Commissioner of Health to thoroughly investigate the possibility of giving acupuncturists formal recognition in society. On the other hand, an Attorney General's opinion was filed in 1975 declaring that, "Based upon a review of the nature of acupuncture, the statutory provision stating what constitutes the practice of medicine, and Minnesota Supreme Court decisions and authorities of other states, we conclude that the practice and use of acupuncture for a fee does constitute the practice of medicine." The formal position of the Minnesota Medical Association is in alignment with that legal opinion. Further, the MMA and the AMA believe that the practice of acupuncture in the United States is still in the experimental stages and should thus reside under the purview of physician designed medical



research.

Yet the meetings go on at the Minnesota Department of Health to determine what kind of credentialing would be appropriate for lay people who practice acupuncture. Is acupuncture the practice of medicine or not? Will the answer be determined by HSOAC, the Commissioner of Health or the Attorney General's office and/or the courts? The meetings go on.

### Department of Legislative Affairs

#### *Chiropractic Blood Drawing Issue Goes to Judge*

Briefs in the case of Board of Medical Examiners versus Thomas E. Murr, D.C. were filed with the Dakota County Judge Robert J. Breunig on October 8, 1980. The Board is asking that Dr. Murr be enjoined from drawing blood since the chiropractor indicates his intention to continue to do so absent a court order.

The Attorney General's brief argues the Board's position that:

- \* Drawing blood for the purpose of diagnosing human conditions clearly constitutes the practice of medicine.
- \* Drawing of blood is outside the scope of chiropractic practice.
- \* Case law strongly supports the position that blood drawing is outside the scope of chiropractic practice and constitutes the unauthorized practice of medicine.

John Brevieu, Special Assistant for Attorney General Warran Spannaus, supplemented the Board's brief with various affidavits. Merle S. Mark, M.D., Minneapolis, Fellow of the



Staff of the MMA Division of Socio-Economic Affairs met on September 24, 1980 with the Mayo Clinic Public Affairs Committee to discuss legislative, health planning and other socio-economic issues. Pictured from left to right are: G. R. Diessner, M.D., Mayo Clinic, AMA Delegate; Robert K. Smoldt, Mayo Clinic, Division of Administrative Services; Howard M. Winholtz, Executive Director, Methodist Hospital, Rochester; Luther E. Boie, Mayo Clinic Business Office; J. A. Gibilisco, D.D.S., Mayo Clinic, Department of Dentistry; Jane Campion, St. Mary's Hospital, Rochester; Greg Orwoll, Mayo Clinic Legal Counsel; George A. Cole, M.D. Mayo Clinic, MMA Trustee; Lynn R. Gruber, Director MMA Department of Medical Services and Research; Charles W. Wiger, Director MMA Department of Legislative Affairs; George C. Lohmer, Jr., Director MMA Department of Health Planning. Also participating but not shown were: M. G. Brataas, Chairman, Mayo Clinic Division of Public Affairs Services; A. Russell Hanson, Chairman, Mayo Clinic Division of Educational Administrative Services; R. H. Ferguson, M.D., Mayo Clinic Board of Governors; E. D. Henderson, M.D., Mayo Clinic Department of Orthopedics; Donald W. Olson, Mayo Clinic Governmental Affairs Office; and James H. Sova, Assistant Executive Vice President MMA Division of Socio-Economic Affairs.

The meeting provided an opportunity for MMA staff to discuss programs and explore ways in which both organizations can work more closely together in areas of mutual concern.



American Academy of Family Physicians, described the several techniques used to draw blood. The rationale for and use of biomedical testing, especially blood testing, was discussed by B. F. Fuller, M.D., White Bear Lake. Dr. Fuller, Board certified in internal medicine, is a former professor of medicine at the University of Minnesota and author of numerous publications. Dr. Fuller concludes that the value and reliability of any test relies on the ability of the clinician to assess the test performed. A chiropractor would have a low predictive value and add considerably to the cost of patient care and the risks patients assume.

Of particular value to the Board's position is the affidavit of A. V. Anderson, M.D., D.C. Dr. Anderson practiced chiropractic in the Minneapolis-Richfield area for 10 years and since 1979 has been licensed to practice medicine in Minnesota. Dr. Anderson feels that drawing blood is not necessary to determine the presence of a chiropractic condition and that chiropractic school textbook training does not provide adequate preparation to accurately diagnose medical conditions. Dr. Anderson is the medical director of the Pain Assessment and Rehabilitation Center in Golden Valley.

MMA members should note the contributions of these several MMA members whose affidavits supplement and support the Board of Medical Examiner's argument.

Reply briefs by both parties are due on October 22, 1980. Attorneys will present oral arguments and the judge will render a decision, without hearing any testimony, by the end of November. It is anticipated that the losing party will appeal the decision to the Minnesota Supreme Court. In that event, final resolution of the issue will not be until mid-1981 unless chiropractors succeed in answering the question in the legislature first.

### **Department of Health Planning**

#### *Health Board's Phase III Report Remanded for Further Study*

The Human Resources Committee of The Metro Council on October 6, 1980, remanded the Health Board's Phase III Report on Hospital Long Range Planning. In remanding the report the Human Resources Committee directed the Health Board to take into consideration a Minority Report developed and signed by 11 Health Board members. The Phase III Report states which hospital services meet Health Board guidelines *and* are consistent with its goals. The services reviewed are pediatrics, perinatal services, open heart surgery, cardiac catheterization, megavoltage radiation therapy, and computed tomography scanning.

The Minority Report as presented by Paul Bowlin, M.D., recommended that community pediatric and obstetric services are not specialized but rather "core" services and should be deleted from the Phase III Report because this Report discusses only specialized services. Additionally, the Health Board should also address through a multi-disciplinary Task Force how to plan for "core" hospital services. The Minority Report was signed by Stanley Antolak, M.D., Jean Blum, Paul Bowlin, M.D., Carol Erdahl, Joseph Kiser, M.D., Steve Kumagai, Harry Lemieux, Nancy Olkon, Paul Rebelein, Jean Smelker, M.D., and Mary Zagaros.

The Physicians' Metro Health Force (PMHF) at the September 24, 1980 Health Board meeting strongly voiced its concern over the inclusion of community based pediatrics and obstetrics in the Phase III Report stressing the impact designation would have on family practice and the viability of community hospitals. Copies of either the PMHF testimony or the Minority Report are available from the MMA Dept. of Health Planning.



# Minnesota Medical Association

## CME in Minnesota

*An ongoing calendar of scheduled CME programs as well as important holidays, state and national medical meetings and other important dates extending into the future will be maintained in the MMA office. CME planners are encouraged to contact the office when planning future programs so as to avoid scheduling conflicts.*

Information for each entry below is arranged as follows: Name of program; Primary sponsor; Location; Date; Contact person.

Stuart V. Thorson, M.D., Chairman  
Subcommittee on CME Resources

### November, 1980

Fall Scientific Program; MN Society of Anesthesiologists; L'hotel de France, Mpls.; Nov. 1; CONTACT David Byer, M.D., 2001 1st St. S.W., Rochester, MN 55901, 507/286-8701.

Workshop on Heart Attack Prevention; U of M Medical School; Spring Hill Center, Wayzata; Nov. 4-6; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

Neonatal Resuscitation; North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 6; CONTACT Mark Bixby, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

Current Topics in Pulmonary Pathology; U of M Medical School; U of M Mpls.; Nov. 6-7; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

Semi-annual Meeting; Minnesota Surgical Society; St. Paul Arts & Sciences Museum, St. Paul, November 7; CONTACT David Culligan, M.D., Suite 707 Gallery Medical Plaza, 17 W. Exchange St., St. Paul, MN 55102, 612/227-7564.

Update in Oncology for Primary Care Physicians; American Cancer Society, MN Div. Inc.; Radisson Hotel, St. Paul; Nov. 7; CONTACT Caryl Range, 2750 Park Ave., Mpls., MN 55407, 612/871-2111.

Advanced Cardiac Life Support Course; North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Nov. 7-8; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

Update in Cardiology; Mayo Foundation; Mayo Clinic, Rochester; Nov. 9; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

Clinical Reviews; Mayo Foundation; Mayo Clinic, Rochester; November 10-12; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

Basic Cardiac Life Support; November 12-13; see December 10-11

Ophthalmology for Primary Care; U of M Medical School; Sheraton Ritz Hotel, Mpls.; Nov. 14-15; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

Practical Therapy of Malignant Disease; Duluth Clinic LTD.; St. Mary's Hospital, Duluth; Nov. 15; CONTACT J. G. Brueggemann, M.D., Dir. of Medical Education, Duluth Clinic, LTD., 400 E. 3rd St., Duluth, MN 55805, 218/722-8364.

Endocrinology; Central Mesabi Medical Center; CMMC; Nov. 19; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.

"Infectious Disease — Adult & Pediatrics" (MAFP Cyclic Core); St. Joseph's Hospital; St. Joseph's, Brainerd; November 19; CONTACT Mark Muesing, M.D., 303 Kingwood, Brainerd, MN 56401, 218/829-3568.

Nordic Sports: A Scientific Approach; U of M Medical School; Mt. Telemark, WI; Nov. 20-23; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### December, 1980

Thirteenth OB-GYN Symposium; North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; Dec. 5; CONTACT Milton Baker, M.D., 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

Winter Meeting, MN Obstetrical & Gynecological Society; North Memorial Medical Center, Mpls.; Dec. 6; CONTACT Richard Bendel, M.D., Hennepin County Medical Center, 701 Park Ave. S., Mpls., 55415, 612/347-2750.

Basic Cardiac Life Support; North Memorial Medical Center, Mpls.; December 10-11; CONTACT William Nelson, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

New Concepts of Otolological Surgery and Clinical Problems in Otitis Media; U of M Medical School with Lions International Hearing Center-Mpls., Chilean Medical Association, Chilean Society of Otolaryngology; Carrera Hotel, Santiago, Chile; Dec. 11-13, CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

Oncology; Central Mesabi Medical Center; CMMC, Hibbing; Dec. 16; CONTACT George Marking, M.D., Mesaba Clinic, Hibbing, MN 55746, 218/262-3441.


C.P.R. Certification (MAFP Cyclic Core); St. Joseph's Hospital; St. Joseph's, Brainerd; December 16; CONTACT Mark Muesing, M.D., 303 Kingwood, Brainerd, MN 56401, 218/829-3568.





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**DRUG INTERACTIONS:** The CNS depressant effects of Empirin with Codeine may be additive with that of other CNS depressants. See WARNINGS.



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## CME IN MINNESOTA

### January, 1981

**Winter Seminar; MN Academy of Family Physicians;** Puerta Vallarta, Mexico; Jan. 16-26; CONTACT Chari Konerza, Exec. Dir., MAFP, 8455 Flying Cloud Drive, Eden Prairie, MN 55344, 612/944-3585.

**Surgery (MAFP Cyclic Core);** St. Joseph's Hospital; St. Joseph's, Brainerd; January 15; CONTACT Mark Muesing, M.D., 303 Kingwood, Brainerd, MN 56401, 218/829-3568.

**Management of Common Office Problems;** St. Luke's Hospital, Duluth; Vail, Colo.; January 18-20; CONTACT Arthur C. Aufderheide, M.D., St. Luke's Hospital, 915 East First Street, Duluth, MN 55805, 218/727-6636, Ext. 5660.

### February, 1981

**"Family Practice Review:** Update 1981; U of M Medical School; Radisson Hotel, St. Paul; February 2-7; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Urology (MAFP Cyclic Core);** St. Joseph's Hospital; St. Joseph's, Brainerd; February 11; CONTACT Mark Muesing, M.D., 303 Kingwood, Brainerd, MN 56401, 218/829-3568.

**"Adult Pharmacology";** U of M Medical School and School of Pharmacy; U of M Mpls.; February 18-19; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**Principles and Practices of Palliative Care;** Hospice St. Paul; Location to be announced; February 20; CONTACT Jan Williams, Hospice St. Paul, 559 Capitol Blvd., St. Paul, MN 55103, 612/221-2235.

**"Practical Otolaryngology Update";** U of M Medical School; L'hotel de France, Mpls.; February 27-28; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

### March, 1981

**"Annual Psychiatry Update";** U of M Medical School; U of M Mpls.; Mid March; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**"Sports Medicine Symposium";** North Memorial Medical Center; N. Mem. Med. Ctr., Mpls.; March 20; CONTACT Glenn Gostick, 3220 Lowry Ave. North, Mpls., MN 55412, 612/588-0616.

**Physical Medicine & Rehabilitation (MAFP Cyclic Core);** St. Joseph's Hospital; St. Joseph's Brainerd; March 12; CONTACT Mark Muesing, M.D., 303 Kingwood, Brainerd, MN 56401, 218-829-3568.

**Seminar for Directors of Medical Education;** MMA; Spring Hill Center, Wayzata; March 27-29; CONTACT Teresa Rogstad, Rm 400, 2221 University Ave. S.E., Mpls., MN 55414, 612/378-1875.

### April, 1981

**"Ninth Annual Symposium Pediatric Challenges for Primary Care Physicians";** Mpls. Children's Health Center; Mpls. Children's Hlth. Ctr.; April; CONTACT Daniel P. Kohen, M.D., 2525 Chicago Ave., Mpls., MN 55404, 612/874-6238.

**"Infectious Diseases";** Duluth Clinic, LTD St. Mary's Hospital, Duluth; April; CONTACT J.G. Brueggemann, M.D., Dir. of Medical Education, Duluth Clinic, LTD., 400 E. 3rd St., Duluth, MN 55805, 218/722-8364.

**Annual Spring Refresher; MN Academy of Family Physicians;** Radisson South, Mpls.; April 8-10; CONTACT Chari Konerza, Exec. Dir., MAFP, 8455 Flying Cloud Drive, Eden Prairie, MN 55344, 612/944-3585.

**"Ophthalmology Specialty Course";** U of M Medical School; Sheraton Ritz Hotel, Mpls.; April 13-14; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

**"Pediatric Days";** Mayo Foundation; Mayo Clinic, Rochester; April 23-24; 10 hrs.; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

**Annual Allergy and Immunology Course;** U of M Medical School; Mayo Memorial Aud., Mpls.; April 30-May 2; CONTACT CME, Box 293 Mayo Bldg., 420 Delaware St. S.E., Mpls., MN 55455, 612/373-8012.

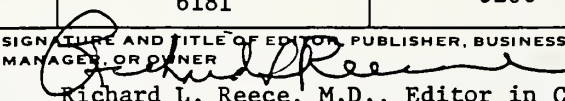
### May, 1981

**"Practice of Internal Medicine";** Mayo Foundation; Mayo Clinic, Rochester; May 4-8; CONTACT Postgraduate Courses, Room 720 Plummer Bldg., Mayo Clinic/Mayo Foundation, Rochester, MN 55901, 507/284-2085.

For further information on the above or future CME programs, contact Teresa L. Rogstad, Director, Department of CME & Program Services, Minnesota Medical Association, Suite 900, American National Bank Building, 101 East 5th Street, St. Paul, Minnesota 55101 (612/222-6366).

**Minnesota Medical Association  
128th Annual Meeting  
May 20-22, 1981  
Radisson South Hotel  
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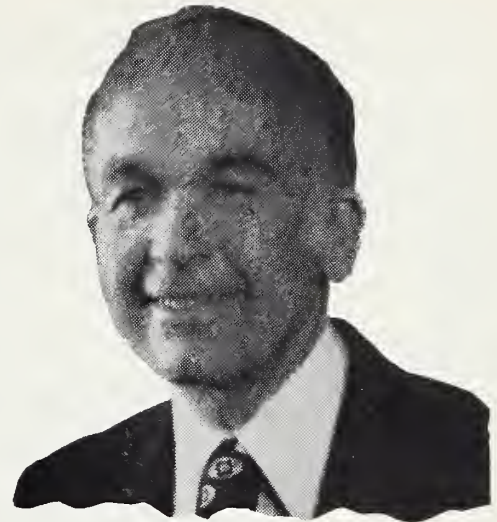
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# President's Letter



## Running

In the July 1979 issue of *Minnesota Medicine*, our distinguished editor, Richard Reece, wrote an editorial titled "How to Avoid Running". Although it was crafted cleverly, it was basically antirunning.

As a runner I have long wanted to reply. Our readers may want to know how I distinguish "running" from "jogging". The latter is a term of opprobrium for some in running circles. The distinction that I accept is that one is running when he or she averages less than ten minutes per mile. By that definition, I am a runner.

It is quite apparent that Editor Reece, like so many other nonrunners, does feel guilty about his sedentary habits. Early in his editorial he says: "You don't have to run, and you don't have to apologize for not running". And if you don't feel guilty about it, you don't have to write an editorial on the subject.

I don't wish to get metaphysical about running as George Sheehan does, but nothing concentrates my mind, uplifts my spirits, or makes me feel better than running. I run when I travel, and those runs remain the clearest memories of my trips.

Sheehan describes morning, noon, and evening runners. I prefer the morning. There is nothing more wonderful for me than to run on a still, clear morning and see the sun rise over the mountains, reflect off the ocean, or make a wheat field appear golden. Running in a light warm rain or fine snow can be exhilarating.

I have run competitively once and probably won't again. For me competition when I run is unnecessary.

Editor Reece and others of his persuasion might find that they too could get hooked on running. Don't knock it until you try it!

John K. Meinert, M.D.  
President  
Minnesota Medical Association

*Editor's footnote: I have tried it. In college, I won six letters in track and cross country. My best times were 49.5 for the 440, 1:55 for the 880, and 4:20 for the mile. I do not now run, but I am not sedentary. I simply prefer a 45-minute walk each evening to running. Running, as Doctor Meinert rhapsodically describes, has its ecstasies. But, as I vividly recall, it has its agonies too. Running is partly pain; walking is pure pleasure.*



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**Contraindications:** Anusol-HC Suppositories and Anusol-HC Cream are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

**Warnings:** The safe use of topical steroids during pregnancy has not been fully established. Therefore, during pregnancy, they should not be used unnecessarily on extensive areas, in large amounts or for prolonged periods of time.

**Precautions:** Symptomatic relief should not delay definitive diagnoses or treatment.

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# Editor's Notebook

## Christmas Cheer

### Thoughts from a Medical School Reunion

*"At Christmas play and make good cheer,  
For Christmas comes but once a year."*

Thomas Husser.

A Hundred Good Points of Husbandry. 1557

Durham, North Carolina — I have returned here for the 20th reunion of the 1960 Duke University Medical School class. I am ensconced in my motel room, rushing to meet a deadline. Deadlines have a way of concentrating your mind. Right now, I am gnawing on the nub of a pencil, musing about what I'm going to write for Minnesota readers. That isn't easy under these conditions. The thermometer this November day will hit 80; and the Carolina leaves retain their autumn brilliance.

Under these less than ideal writing circumstances, I have settled on these three points of departure: (1) contrasting the medical scene here at Duke to that of Minnesota; (2) commenting briefly on what has happened in the 20 years since I graduated; and (3) explaining why I feel so full of good cheer this particular holiday season.

### Durham and Duke

Durham, a sleepy tobacco town of about 95,000, is not at all like Minneapolis. Durham's downtown is dying while Minneapolis's inner core is booming. Durham is primarily a one-industry town, making many of America's cigarettes. Minneapolis is the diversified home of at least 25 major corporations, each making over one billion dollars a year. Durham is relatively unsophisticated and lacks a single first class restaurant. Minneapolis has achieved a reputation among sophisticates and boasts a score of first rate cuisines.

But in medicine, there are parallels. In many ways, Duke University Medical Center reminds me of a southern Mayo Clinic. Like Mayo, Duke sits like a medical colossus in a relatively remote and rural region, removed from any nearby competing metropolitan centers. Like Mayo, Duke has a large private diagnostic clinic, which is capable of mobilizing an awesome medical talent to focus on almost any problem. Like Mayo, Duke has small medical school classes and stresses excellence (medical school deans recently selected it as the second best medical school, behind Harvard). Like Mayo, Duke depends heavily on managerial skills and discipline to keep itself at the pinnacle of prestige. And, like Mayo, Duke simultaneously cultivates a rich mix of referrals from its home state, the rest of the United States, and from abroad.

### The Last Twenty Years

What has happened to our class of about 70 since we graduated? Most of us are scattered around the Eastern seaboard and south. Most of us are specialists. Of the 35 or so at the reunion, only one is in family practice. This is quite a switch from the current University of Minnesota Medical School. In its 1979 class, 75 percent went into primary care, i.e. family practice, internal medicine, or pediatrics. Most of my Duke class are in solo private practice, small group practice, or in academic or government medicine. None, to my knowledge, practice in large multispecialty groups, in large single specialty groups, or in HMOs. In the South, the HMO concept is still largely alien outside such metropolitan areas as Washington, D.C. or Winston Salem, North Carolina.



And what has happened to Medicine since 1960? Well, frankly, it has become a huge growth industry, with the government now paying about 40 percent of the freight. As I was leaving Minnesota, I took along in my briefcase the most recent issue of the *Mayo Clinic Proceedings*. In one article are two revealing Tables contrasting the division and growth of health care costs since 1960.<sup>1</sup> Here are excerpts from those tables.

TABLE 1  
Division of US Health Care Dollar

	1960	1978
Hospital care .....	32 cents	40 cents
Physicians' services .....	21	18
Dental services .....	7	7
Drugs, eyeglasses, and appliances .....	16	10
Research .....	2	2
Public health and government .....	5	8
Other .....	17	15

TABLE 2  
Expenditure Growth by Sector (\$billion)

	1960	1978	Annual % change
Government-financed health care .....	\$ 5.3 billion	\$ 72.2 billion	12.8
Privately financed health care .....	18.8	110.8	9.5
Hospital care .....	8.5	76.0	11.2

Physicians, of course, have shared in the health care prosperity engendered by this growth. But not as much as one might think. From 1959 to 1977, the median unincorporated physicians income before taxes increased 4.9 percent per annum, compared to an increase of 6.2 percent for the total US average worker's compensation.<sup>2</sup>

### National Health Not Inevitable

Even in the face of increased government financing, American Medicine has not become "socialized," which would probably have surprised most of us in 1960 if we were looking ahead to 1980. Indeed, most of the doomsayers and naysayers have been telling me ever since 1960 that a National Health Service was "inevitable". Given the heterogeneity of the American people, the pluralistic health system, and the American belief in freedom to pursue preferences for residence, work, and income, I was never convinced a National Health Service, at least anything remotely resembling the British system, would come to pass. I have said so in many editorials.

### New Administration and New Goals

Now that we have an Administration in Washington committed *not* to introducing National Health, I am more persuaded than ever that a distinctly *American* solution to our goals of quick access, high quality, controllable costs, and fair equity will evolve.

At least part of this solution towards meeting these goals will entail "competitive medicine", which is distinctly American. As Duncan Neuhauser, a health care economist formerly of Harvard and now of Case Western Reserve, said recently: "In my opinion, this competitive approach, as advocated by Alain Enthoven, Paul Ellwood, Walter McClure and others, is the most likely future direction for American medical care. It is a striking departure from the way in which other countries, including England, Sweden, Canada, and the Soviet Union, organize and pay for health care . . . Unlike Scandinavians and the British, Americans are more enthusiastic about the virtues of the free market in general and medical care competition in particular."<sup>3</sup>



### Christmas Cheer

Perhaps this distinctly American turn in the direction of our health system and in our politics is why I'm so full of good cheer as the Christmas season approaches. With Christmas just around the corner, I'm feeling as ebullient as the current Dow Jones averages. I'm so upbeat, I am going to offer two cheers for America's prospects for the 1980s.

Why not three cheers? I said I was optimistically enthusiastic. I did not say I was daft. To give three cheers for anything when the economy is still lagging, inflation raging, and productivity sagging is misplaced enthusiasm.

Still, if you'll forgive the Christmas cheer, I feel America has regained her balance and her sense of positive vision. What defeated President Carter was not that he was too liberal but that he was too negative. Americans wanted to hear not what they are but what they could be. Carter blamed our problems on our "malaise of spirit" — our self-indulgence, our profligate life style, our moral degeneration, our inability to sacrifice, our unwillingness to accept our lowered place in the sun. He told us our cruel system was "ripping off" the poor, and our businesses were making "obscene profits." These negative preachments turned off a lot of Americans.

### Christmas Tide

As a people, we do not want shame or guilt. Instead we want an optimistic vision — a return to the viewpoint John Kennedy so eloquently expressed when he said: "A rising tide lifts all boats." What we need is a new spirit, a renewed confidence in our abilities and energies, and a new dedication to incentives and growth. I believe the tremendous investment Americans have made in their educational system, in new knowledge, and in the health system these last 20 years is about to pay off. America is bubbling with creativity and enterprise, has a new generation of capable young leaders in the wings, and is about to burst forth with the technological and social inventiveness for which she used to be so well known. Merry Christmas and a Happy New Future.

A handwritten signature in black ink that reads "Richard L. Reece" followed by a stylized flourish.

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# Editorial

## Symposium on Echocardiography

Zeev Vlodaver, M.D.\*  
Guest Editor

**T**HIS SYMPOSIUM was organized under the auspices of the Health Central Institute and the Department of Medicine at Unity Hospital.

The contributors discussed significant aspects of the current status of our knowledge in the field of echocardiography. Since the primary work of Edler and Hertz in Sweden, the clinical application of echocardiography in practical cardiology has continued to grow.

In 1954, these investigators used a sonar device borrowed from a local shipyard to record the movements of the mitral valve. Two years later, in 1956, Edler published his findings on 100 patients with mitral stenosis. In the 20 of these patients that had undergone operation, the investigators found good correlations of their echocardiographic findings with direct observation of the mitral valve. Shortly thereafter, in 1957 in Minnesota, Wild, Crawford and Reid, after working for several years with ultrasound, published their experimental work on echocardiography done on the excised fresh heart. They obtained an image of the infarcted area of the posterior wall of the heart by sweeping the sound beams through the tissue.

Meanwhile, the technique of Edler and Hertz of recording echocardiograms in human subjects was adopted by other workers in Europe and the United

States. In the United States, Joyner, Reid and Bond of the University of Pennsylvania in 1962 presented their findings on 200 patients. A survey of the publications on ultrasound as applied to the heart in the 15 year period from 1955 to 1970 revealed relatively few publications. These concentrated mainly on movement of normal aortic and mitral valves and the diagnoses of pericardial effusion and mitral stenosis. The extensive application of echocardiography since 1970 to a large number of patients expanded our knowledge of clinical echocardiography. In the last five years there have appeared hundreds of publications on echocardiography with an emphasis on the various types of cardiomyopathies, assessment of left ventricular function, bacterial endocarditis, prolapse of the mitral valve and the dynamics of the prosthetic valves.

The use of echocardiography now includes emergency evaluation of acute myocardial infarction and its complications and the diagnosis of heart disease in infants and children. New techniques include real time two dimensional and multiscan echocardiography.

The contribution of echocardiography to the diagnosis of heart disease, its nature and complications has achieved major proportion. Further investigation will undoubtedly expand the diagnostic capabilities and have an increasingly greater impact on clinical cardiology than even exists today.

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**Minnesota Medical Association  
128th Annual Meeting  
May 20-22, 1981  
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Bloomington, Minnesota**



# Anatomic-Pathologic Foundations for Echocardiography

JESSE E. EDWARDS, M.D.

Highlighted are the anatomic structures and the pathologic processes that are identifiable by echocardiographic study.

Of the pathologic states the various causes of pericardial thickening and effusion are presented. Causes of intracavitary masses are presented.

Emphasis is made of the mitral valve, its appearance both in stenosis and incompetence. Conditions affecting the aortic valve and aortic root are presented as a base line for echocardiographic interpretation of abnormalities.

**T**HE ECHOCARDIOGRAPHIC study of the heart is based upon knowledge of the anatomic structures and their relationships with one another. It is therefore appropriate to review the highlights of these. It is the intention of this presentation to show some abnormalities in the heart and pericardium that have been identified or are potentially recognizable by echocardiography.

## Normal Features

The exterior of the heart is covered by its epicardial

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layer, the so-called visceral pericardium. In the normal, the visceral pericardium is separated by a thin layer of fluid in the pericardial cavity from the parietal layer, the latter being a thin sheet of fibrous tissue.

The ventricles lie inferior to and somewhat more anterior than the atria.

The infundibulum of the right ventricle lies anterior to the ventricular septum and to the subjacent left ventricle and aortic root.

A plane of section through the right ventricular infundibulum and pulmonary valve like that employed in echocardiography traverses the ventricular septum and the inflow portion of the left ventricle anterior to the level of the mitral apparatus (Figure 1 (a)). The

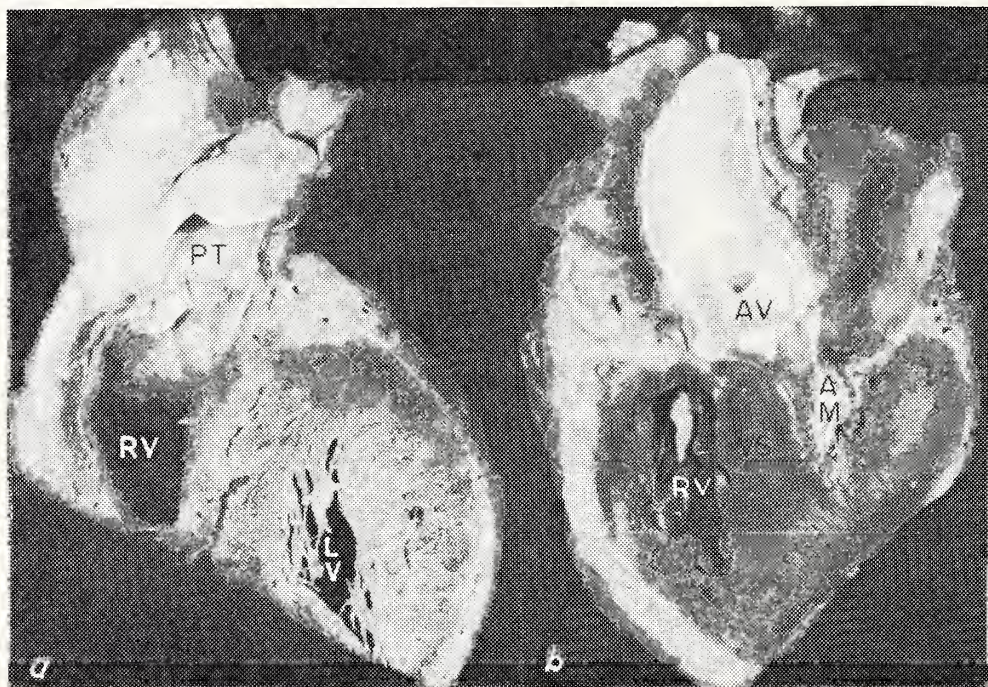


Fig. 1 — Normal Heart. (a) Oblique section through the outflow tract of the right ventricle (RV), pulmonary trunk (PT) and the left ventricle (LV). The latter lies anterior to the level of the mitral valve. (b). A more posterior plane to that shown in a reveals the aortic valve (AV) and its continuity with the anterior mitral leaflet (AM). The posterior mitral leaflet (PM) faces the ventricular septum. RV = inflow portion of right ventricle.



pulmonary valve is separated from the tricuspid valve by the infundibulum.

A more posterior plane of section, one through the aortic valve, exposes the two leaflets of the mitral valve and the left atrium (Figure 1 (b)). This plane of section lies posterior to the level of the right ventricular infundibulum and includes the inflow portion of the right ventricle. It reveals the fibrous continuity between the aortic valve, above, and the anterior leaflet of the mitral valve, below.

Of the two mitral valvular leaflets, the anterior is not only in fibrous continuity with the aortic valve (Figure 2) but in close apposition to the ventricular septum (Figure 1 (b)). This leaflet therefore forms part of the wall of the left ventricular outlet. During ventricular diastole when the mitral valve is open, the anterior leaflet lies close to and may make contact with the ventricular septum. During ventricular systole, the anterior mitral leaflet moves away from the septum to make contact with the posterior mitral leaflet. By this movement, the mitral valve is closed, while the left

ventricular outlet widens for easy expulsion of left ventricular blood into the aorta.

The posterior mitral leaflet is related to the inferior wall of the base of the left ventricle. Its basal attachment is to the mitral annulus, the common meeting place of the left atrium and left ventricle (Figure 1 (b)).

### Pathological States

#### *The Pericardium*

Thickening of the pericardium may result either from material in the pericardial cavity or from thickening of the epicardial layer with tissue of some

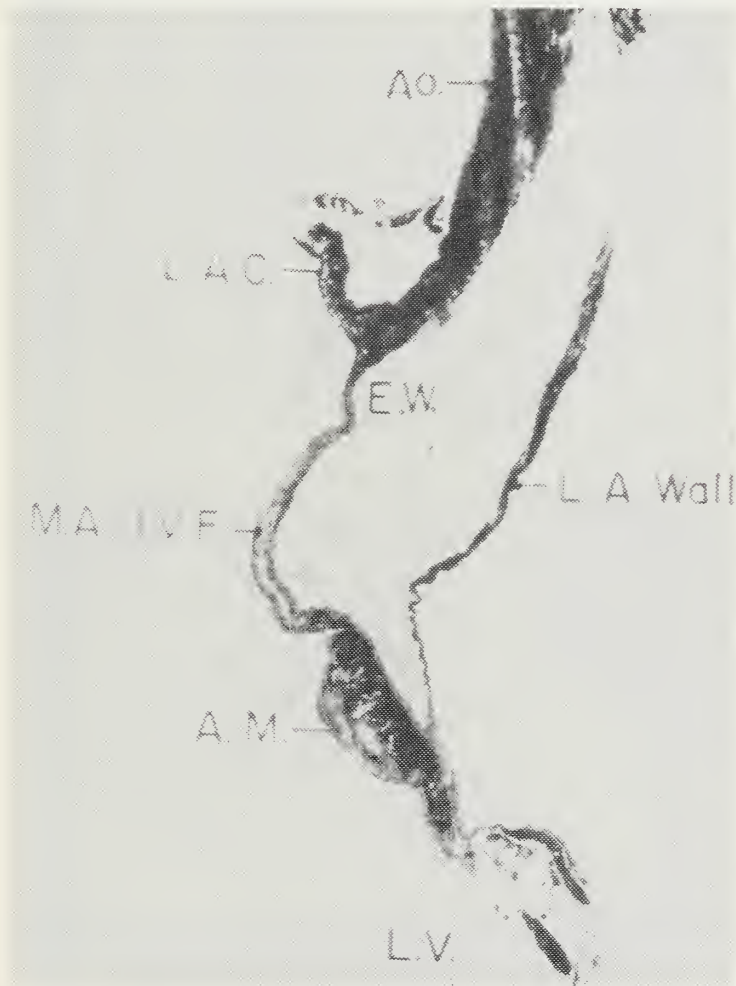


Fig. 2 — Low power photomicrograph of the left aortic cusp (LAC) and the anterior mitral leaflet (AM). The fibrous continuity between the two valves by way of the mitral-aortic intervalvular fibrosa (MAIVF) is shown. The epicardium (EW) is interposed between the mitral-aortic intervalvular fibrosa, anteriorly, and the anterior wall of the left atrium (LA), posteriorly. LV = left ventricular cavity; Ao = ascending aorta. (From Chesler et al.: *Circulation* 37:518, 1968; with permission.)

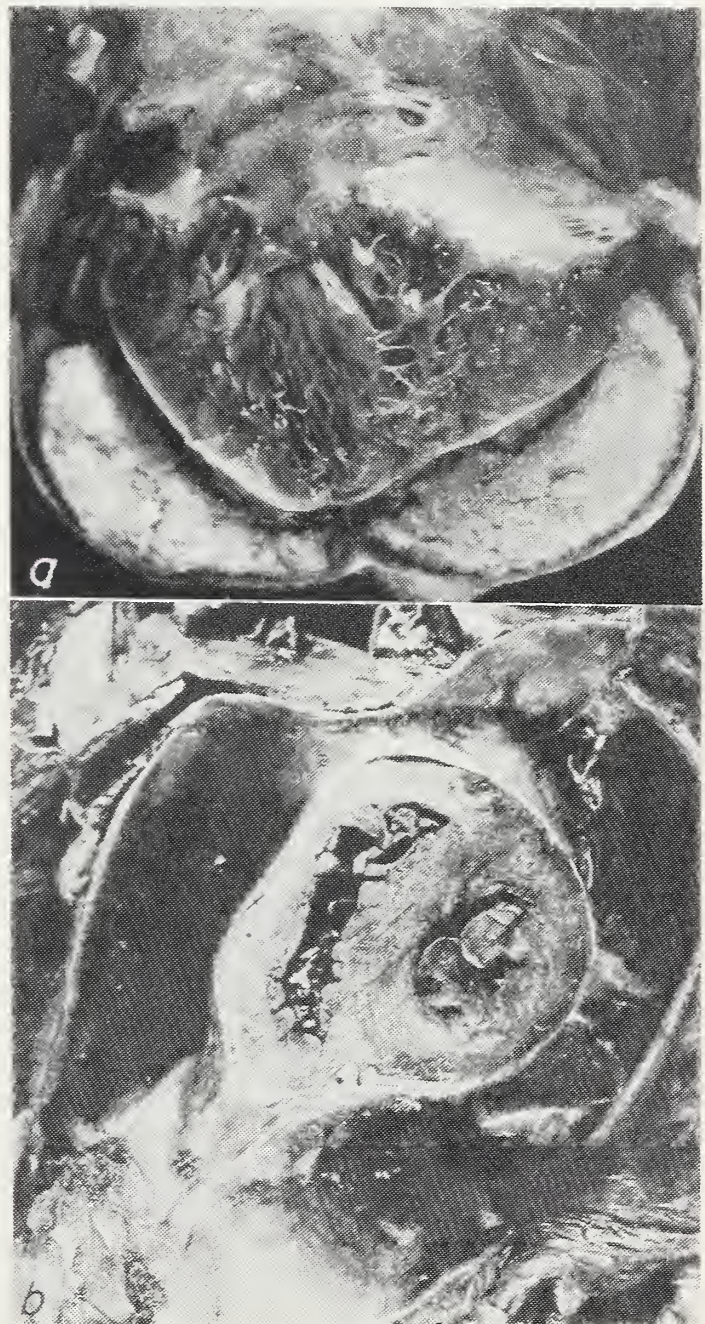


Fig. 3—(a) Extensive fibrinous effusion in the pericardial sac. (b) Cross section of parietal pericardium and the heart in extensive pericardial effusion. One adhesion is present between the visceral and parietal layers of the pericardium (lower part of illustration). (a and b from Edwards: *22Atlas of Acquired Diseases of the Heart and Great Vessels*. Saunders, Philadelphia, 1961, p. 1401; with permission.)



sort.<sup>1</sup> Materials that may accumulate in the pericardial cavity include fibrin, pus, serous fluid, blood and blood clots.

There are many backgrounds for foreign materials entering the pericardial cavity. Fibrinous effusion may

result from acute rheumatic carditis, uremia, lupus, viral infections and surgical intervention upon the heart. Primary and secondary tumors are among other causes. Usually, simple fibrinous deposits do not constitute a layer thick enough to be detected by echocardiography. Rarely, however, this may be the case (Figure 3 (a)). If fibrinous effusion is associated with serous effusion, the pericardial sac may be sufficiently distended as to be appreciated as enlargement of this space (Figure 3 (b)).

Purulent pericarditis, resulting either from direct extension from infection of a contiguous site or from

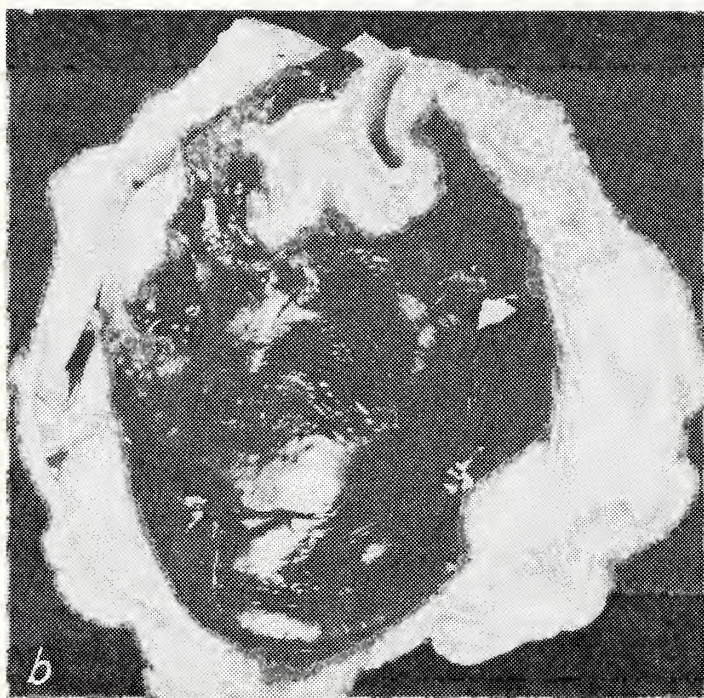


Fig. 4—(a) Hemorrhagic pericardial effusion in a uremic patient who had received dialysis. Between the epicardial wall of the left ventricle and left atrium, on one hand, and the parietal pericardium, on the other, is an accumulation of blood clots. (From Baldwin and Edwards: *Circulation* 53:896, 1976; with permission). (b) Hemorrhagic effusion into the pericardium obscuring the heart in a case of acute myocardial infarction with rupture of the free wall of the left ventricle.

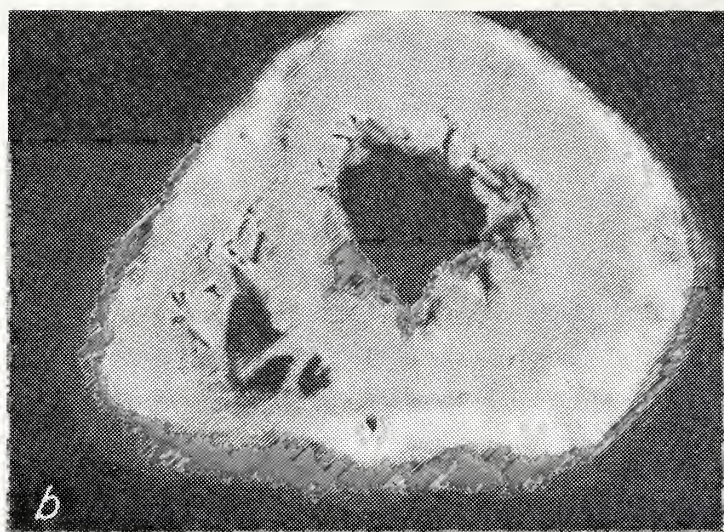


Fig. 5—(a) Chronic fibrocalcific constrictive pericarditis. A shell of dense fibrocalcific material encases the heart. (From Edwards: *Atlas of Acquired Diseases of the Heart and Great Vessels*. Saunders, Philadelphia, 1961; with permission.) (b) Metastatic bronchogenic carcinoma involving the epicardium and the underlying myocardium. Fibrinous pericarditis is also evident. (From Edwards: *Cardiovasc Clin* 4:282, 1972; with permission.)



blood stream dissemination of organisms, yields distention of the pericardial sac of various proportions.

Blood in the pericardial cavity may originate in granulation tissue associated with fibrinous, serofibrinous or purulent pericarditis. The amount of blood varies from giving a slight discoloration of preexisting fluid to gross blood (Figure 4 (a)).

Primary hemorrhage into the pericardial sac results mainly from one of two underlying conditions, namely transmural myocardial infarction with rupture of the free wall of the left ventricle (Figure 4 (b)) or from rupture of the aorta in acute dissecting aneurysm of this vessel.

Tissue that is added to the epicardium so as to be recognizable as pericardial thickening usually not only involves the epicardium but also the pericardial space and the parietal layer of the epicardium. The fibrocalcific constriction upon the heart causing classical chronic constrictive pericarditis is one example (Figure 5 (a)). Others include granulomatous diseases such as active tuberculosis and the granulomas of rheumatoid arthritis. Neoplasms, either primary or secondary, such as carcinomas or leukemias or lymphomas, may cause a solid shell of tissue to encase the heart (Figure 5 (b)).

### *The Right Ventricle*

Variations involving the right ventricle include the

size of the chamber, the thickness of the wall and intracavitary foreign materials.

Enlargement of the right ventricular cavity is one of the features of the failing ventricle or pretricuspid left-to-right shunts. The most highly developed examples of enlargement are seen both in atrial septal defect and in supradiaphragmatic forms of total anomalous pulmonary venous connection. In the stages of these conditions that precede the development of pulmonary hypertension, the wall of the enlarged chamber is not thickened (Figure 6 (a)). When complicating pulmonary hypertension appears, the thickness of the wall increases while some signs of enlargement of the chamber may persist (Figure 6 (b)).

In other conditions involving shunts, mainly ventricular septal defect and patent ductus arteriosus, the state of the right ventricle varies depending upon the caliber of the abnormal communication. In small ventricular septal defect and in classical patent ductus arteriosus, the right ventricle is essentially normal both as to size of cavity and thickness of the wall.

In the same conditions but with openings sufficiently large to be associated with pulmonary hypertension the right ventricular chamber is of normal volume, while the wall is hypertrophied, being similar



Fig. 6—(a) Right atrium and right ventricle in a case of atrial septal defect (previously closed) showing residual enlargement of the right-sided chambers without significant right ventricular hypertrophy. (b) Right atrium and right ventricle in a case of atrial septal defect with pulmonary hypertension. The right ventricular wall is hypertrophied and the cavity is now only slightly enlarged. (a and b from Edwards: *Seminars in Roentgenol* 1:24, 1966; with permission.)



in thickness to that of the left ventricle. A similar state applies in the tetralogy of Fallot, while in pulmonary stenosis with intact ventricular septum the right ventricular wall may exceed the left ventricular wall in thickness.

In various, non-congenital states wherein pulmonary hypertension is present, as in diffuse pulmonary

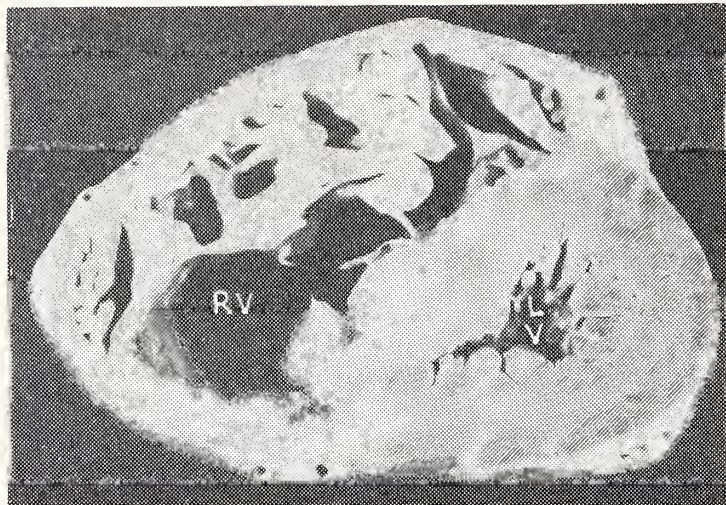


Fig. 7 — Cross section of the cardiac ventricles showing marked hypertrophy of the wall of the right ventricle (RV) in a case of primary pulmonary hypertension of the thromboembolic type. The wall of the left ventricle (LV) is within normal limits.

parenchymal disease and in primary pulmonary hypertension, the primary abnormality of the right ventricle is hypertrophy of its wall (Figure 7). In such states, the size of the chamber is initially normal but may enlarge to some degree if the ventricle fails.



Fig. 8 — Right ventricle in chronic congestive cardiac myopathy. At the apex (right lower portion of illustration) are mural thrombi caught between the muscular bundles.

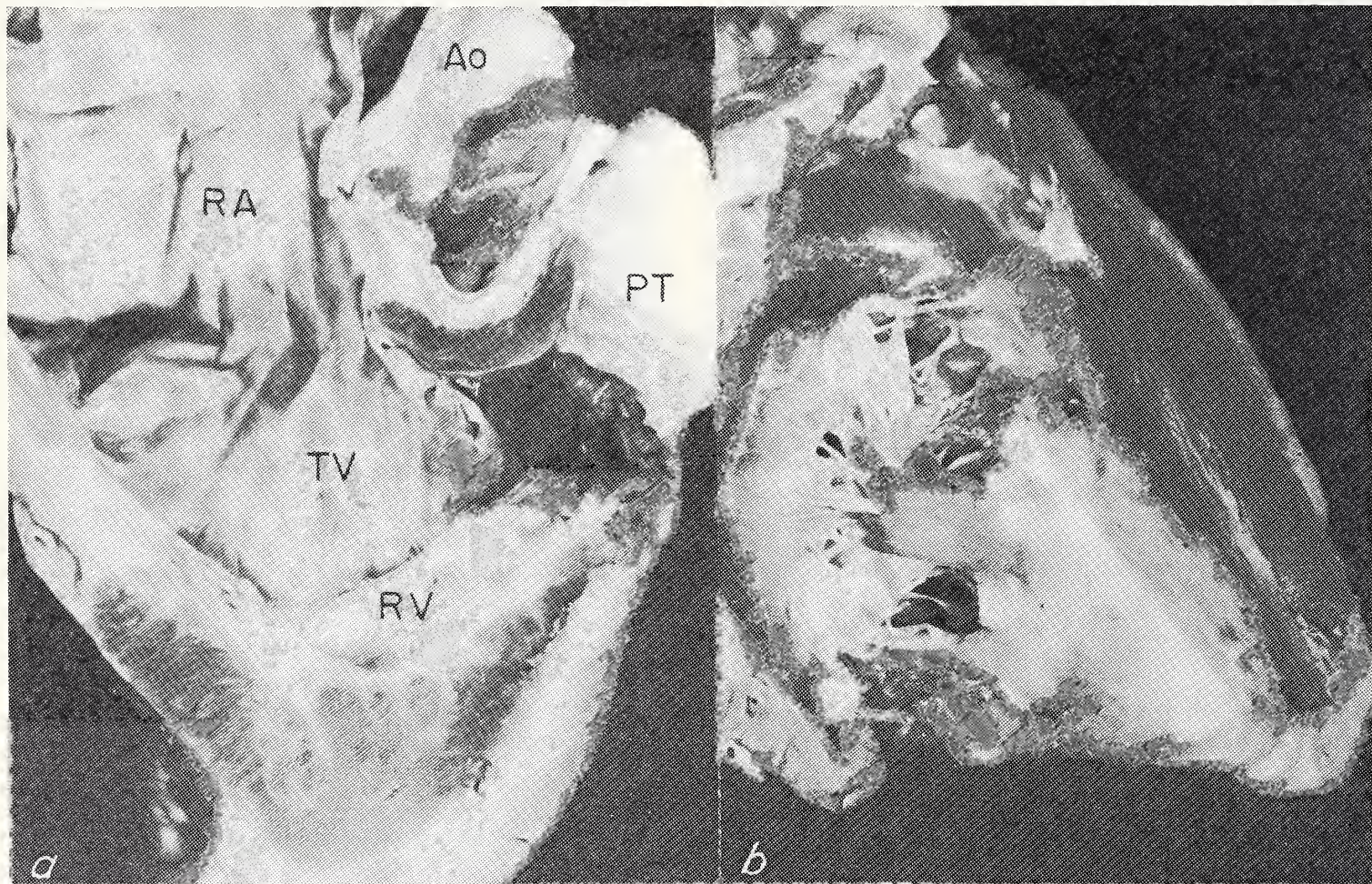


Fig. 9 — Extraneous material in cavity of right ventricle. (a) The inflow portion of the right ventricle has been reduced in size by fibrous tissue which represents organized thrombus in a case of the hypereosinophilic (Loeffler's) syndrome. Elements of the tricuspid valve (TV) are adherent to the thrombus. PT = pulmonary trunk; RV = right ventricle; RA = right atrium; Ao = ascending aorta. (From Hall et al.: *Circulation* 55:217, 1977; with permission.) (b) Metastatic adenocarcinoma which was primary in the endometrium involving the apical portion of the right ventricle with intracavitary growth. (From Edwards: *Cardiovasc Clin* 4:282, 1972; with permission.)



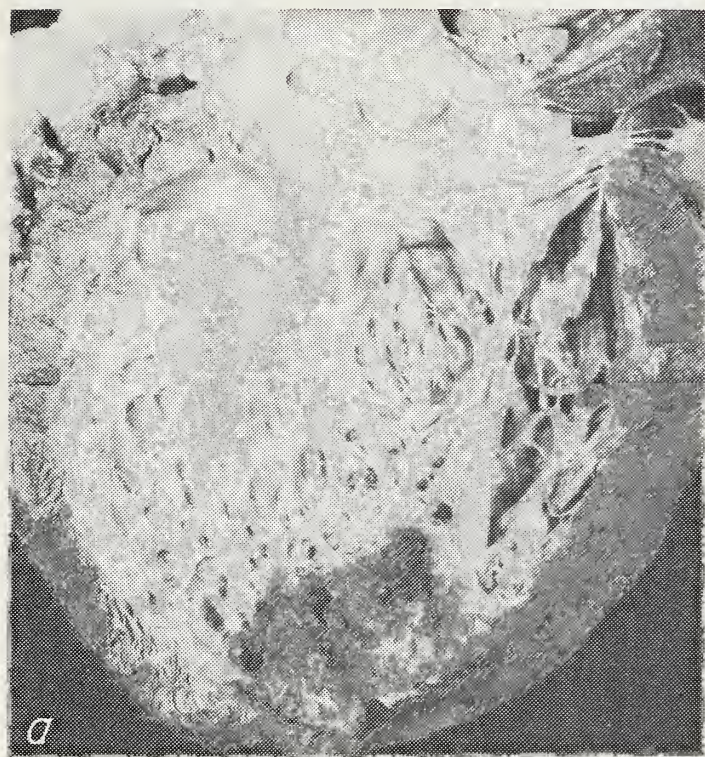


Fig. 10 — Space occupying mural thrombi in left ventricle. (a) From a case of congestive cardiac myopathy. Mural thrombi are present in the apex of the left ventricle (b) The apical third of the left ventricle is filled with thrombi in a case of the hypereosinophilic syndrome. From the same case illustrated in Figure 9(a).

Foreign materials in the right ventricle, exclusive of catheters and electrodes placed in the chamber and their fibrous reactions,<sup>2</sup> include thrombi and tumors.

The most common basis for mural thrombosis of the right ventricle is failure of this chamber for any reason. When present, mural thrombi on such a basis tend to involve the apical half of the ventricle and to be distributed as multiple accumulations among the columnae carnae (Figure 8). Extensive space-occupying thrombosis may involve the right ventricular cavity in the hypereosinophilic (Loeffler's) syndrome (Figure 9 (a)).<sup>3</sup> Tumors either primary or secondary may extend from the wall of the chamber into its cavity (Figure 9 (b)).

#### *Left Ventricle and Ventricular Septum*

Localized loss of muscle in the left ventricular wall through infarction varies in degree. Lesions that are of limited nature may not involve thinning of the wall to a degree that is recognizable as thinning by echocardiography. Yet such areas may exhibit faulty contraction that is potentially recognizable.

Large areas of infarction in the healed stage are associated with degrees of thinning of the wall that may be appreciated by echocardiography. In some cases, such areas may be associated with aneurysm formation either of the true or false variety. Classically, the inlet to a true aneurysm is broad, while that of a false aneurysm is more narrow than the fundus. Characteristically, mural thrombi are contained in left ventricular aneurysms whether true or false in type.

The failing left ventricle has a tendency to develop mural thrombi. These are usually situated at the apex of

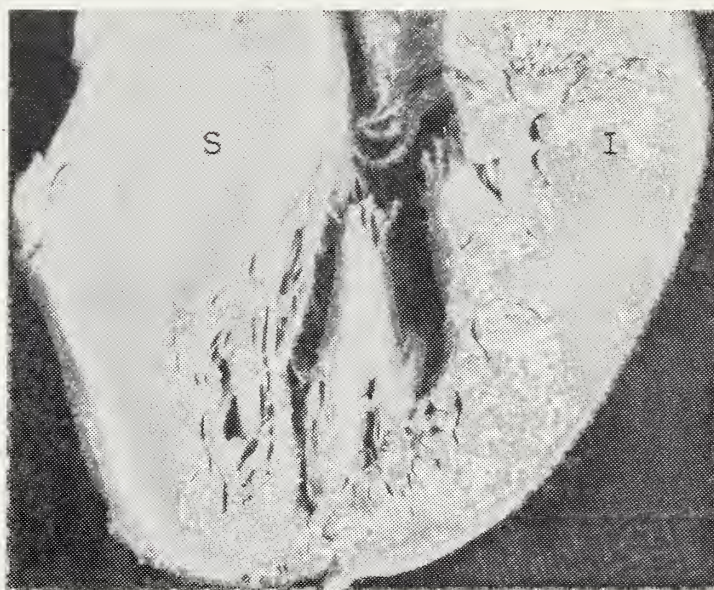


Fig. 11 — Asymmetrical septal hypertrophy. The septal wall of the left ventricle (S) is markedly hypertrophied in its basal half and is thicker than the inferior wall (I) of the left ventricle.



the cavity and occupy space in concert with their size (Figure 10 (a)). Extensive space occupying thrombosis may occasionally be seen either in the failing ventricle or in the hypereosinophilic syndrome (Figure 10 (b)).

The wall of the left ventricle is usually uniform in thickness from one area to another (except at the apex where the wall is classically thinner than elsewhere).

Localized thickening of the ventricular septum is most commonly part of the syndrome of hypertrophic muscular subaortic stenosis, also termed asymmetrical septal hypertrophy. The specific process characteristically involves the basal half of the ventricular septum. This part is significantly thicker than the free wall of the chamber (Figure 11). In the thickened area particularly does the histologically abnormal relationship between fibers and the presence of abnormal fibers characteristic of this condition occur.<sup>4</sup>

#### *The Mitral Valve*

A number of lesions of the mitral valve have the potential of giving abnormal echocardiographic signs. These may be grouped into those with the following characteristics: (1) restricted excursion, (2) excessive excursion, and (3) the presence of extraneous material.

#### *Restricted Excursion*

Restricted excursion of the elements of the mitral



Fig. 12 — Mitral stenosis. The unopened mitral valve is viewed from the left ventricular aspect. The characteristic of fibrosis of the cusps, chordal shortening and interchordal fusion is evident, as is commissural fusion. The latter process is most evident in this perspective at the anterolateral commissure (left side of mitral valve in this view).

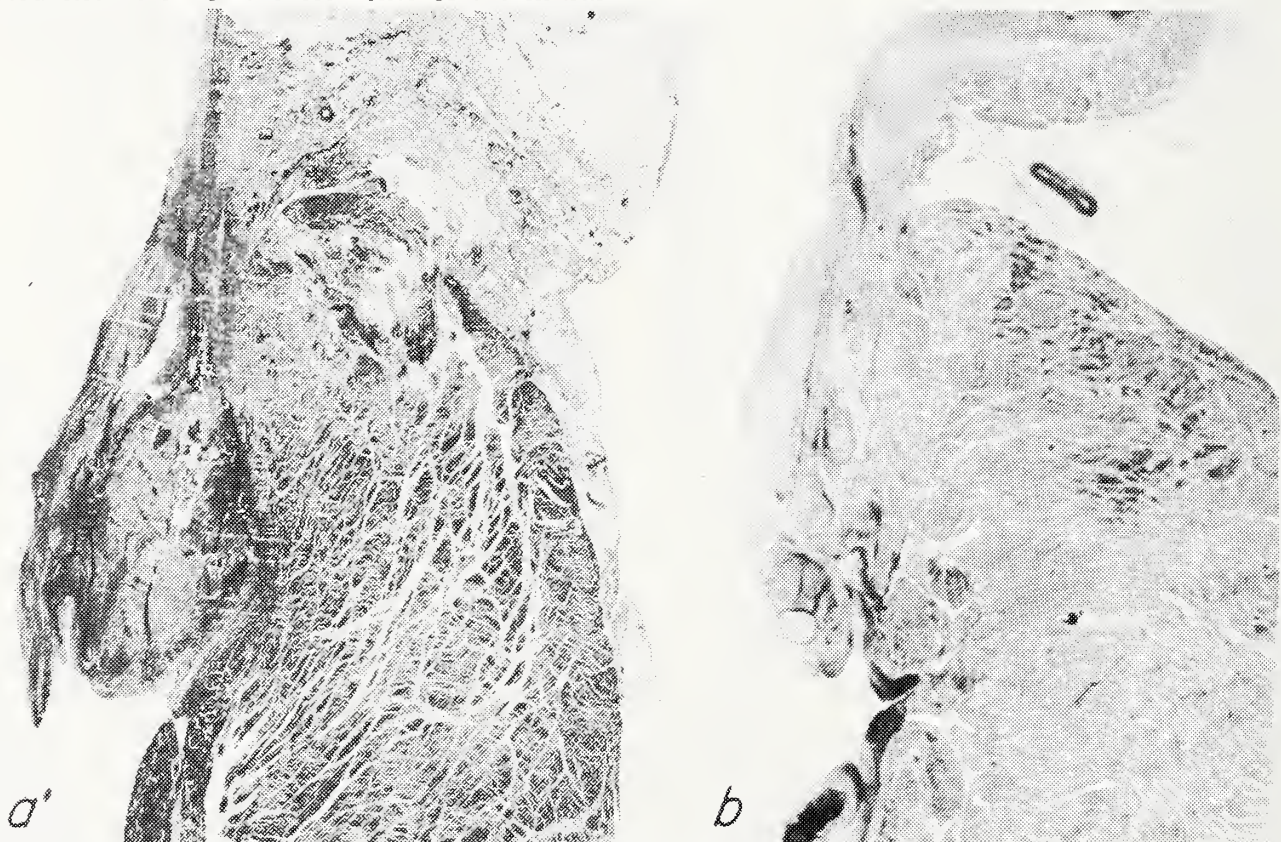


Fig. 13—(a) Low power photomicrograph of left atrium, left ventricle and posterior mitral leaflet in a case of active bacterial endocarditis of the mitral valve. Between the leaflet and the left ventricular wall is a vegetation. H & E; x 3. (b) In a case of healed bacterial endocarditis, the same perspective as shown in (a) reveals that the posterior mitral leaflet is now adherent to the mural endocardium of the left ventricle by fibrous tissue. The latter process is considered to have resulted from organization of a vegetation like that observed in (a). Elastic tissue stain; x 3.



valve may affect either both leaflets or only the posterior one. The classic example of restricted excursion of both leaflets is rheumatic mitral stenosis. This comes about principally by fusion at each of the two commissures. This process binds the two leaflets together so that they cannot exhibit the normal excursions that characterize the cardiac cycle (Figure 12). Shortening of chordae which usually is also present in mitral stenosis is yet another factor that prevents excursion of the leaflets. Secondary calcification may occur in the leaflets and commissures.

Restricted excursion of the posterior leaflet may result from adhesion of this leaflet to the mural endocardium of the left ventricle, from commissural fusion, particularly with calcification and/or shortening of leaflets, or from acquired shortening of the chordae that insert into this leaflet.

Fusion of this leaflet to the left ventricular wall may result from healing of that component of bacterial endocarditis characterized by the formation of vegetations in the angle between the posterior leaflet and the related part of the left ventricular wall (Figure 13).<sup>5</sup> Hypereosinophilic (Loeffler's) syndrome, the process involving the mural endocardium may fuse with the posterior mitral leaflet and immobilize it.<sup>3</sup>

In rheumatic disease that leads to mitral insufficiency the leaflets are shortened and, in some cases, there is also commissural fusion. The latter process, particularly if calcified, may lead to major restriction in movement of leaflet tissue. In cases without

commissural fusion, enlargement of the left atrium may place tensions upon the posterior leaflet so as to immobilize it, yielding a process whereby "mitral insufficiency begets mitral insufficiency".<sup>6,7</sup>

It has been recognized that, in the floppy or

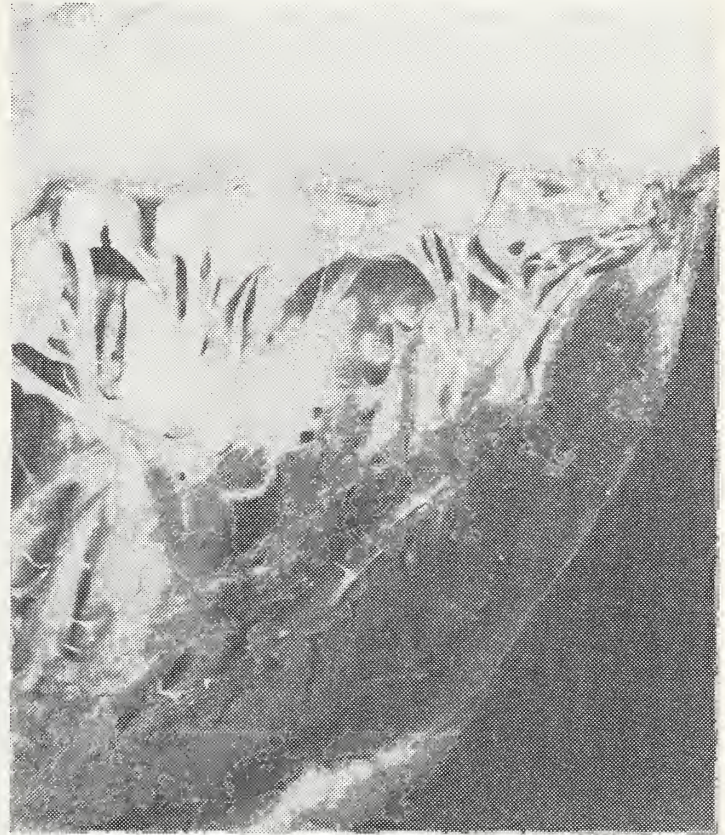


Fig. 14 — Floppy mitral valve in a case of Marfan's syndrome in which death was caused by dissecting aneurysm of the aorta. The lower parts of chordae of the posterior mitral leaflet are encased by fibrous thickening of the mural endocardium of the left ventricle. The chordae are effectively shortened by the process.



Fig. 15 — Floppy mitral valve. (a) The mitral valve is viewed from above. The prolapse of numerous elements of the valve gives a scalloped appearance to the valve in this view. (b) The opened mitral valve from the same specimen as shown in (a) reveals that there is interchordal hooding particularly of the elements of the posterior leaflet (left and right sides of illustration). The anterior mitral leaflet (center of illustration) shows several foci of lesser degrees of prolapse, as well.



prolapsed mitral valve, chordae attaching to the posterior mitral leaflet may cause friction upon, with secondary fibrous reaction of, the left ventricular mural endocardium.<sup>8</sup> In extreme degrees of reaction, chordae may become encased in the reactive fibrous tissue and so become effectively shortened (Figure 14).

#### Excessive Excursion

The most common basis for excessive excursion or

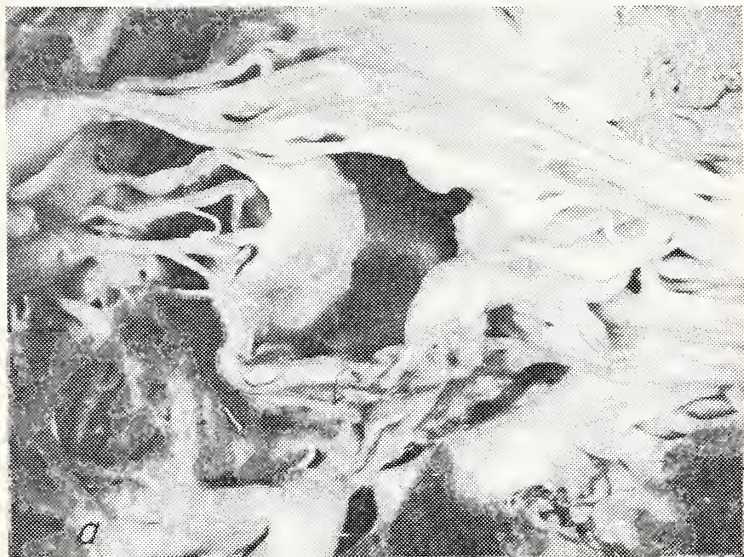


Fig. 16 — Floppy mitral valve complicated by rupture of chordae to the posterior leaflet. (a) The unopened mitral valve viewed from the left ventricular aspect. Attached to the lower (posterior) leaflet are shreds of attenuated and ruptured chordae. The remaining chordae are excessively long. (b) The unopened mitral valve viewed from above from the same case as shown in (a) reveals prolapse of wall of all elements of the valve but with particular prominence of the deformities in that part of the posterior leaflet that is unsupported by chordae (lower part of illustration).

prolapse of the mitral leaflets is the condition variously called prolapsed, floppy, or myxomatous mitral valve, among many other names. In this condition, the characteristic gross change is upward protrusion of those elements of the leaflets that lie between chordal insertions (Figure 15).<sup>9,10</sup> Excessive length of the chordae may also contribute to the prolapse.

Although both of the mitral leaflets may be involved, it is more common that the posterior leaflet show this change and particularly its central portion.<sup>11</sup> When the anterior leaflet is involved, its medial half is more commonly affected than the lateral aspect.

Rupture of mitral chordae allows major prolapse of the mitral valve. Two major types are recognized, one resulting from bacterial endocarditis and the other as a complication of the floppy mitral valve.<sup>12</sup> In the latter situation, it is much more common that the posterior leaflet (particularly its central part) than the anterior leaflet be involved. Rupture of chordae allows greater excursion of the unsupported segment than of the remaining, supported elements of the valve (Figure 16).

Myocardial infarction, particularly of an inferobasal distribution, may lead to inadequate support of the leaflets and consequent prolapse even without rupture of a papillary muscle.<sup>13</sup>

The classical background for rupture of a papillary

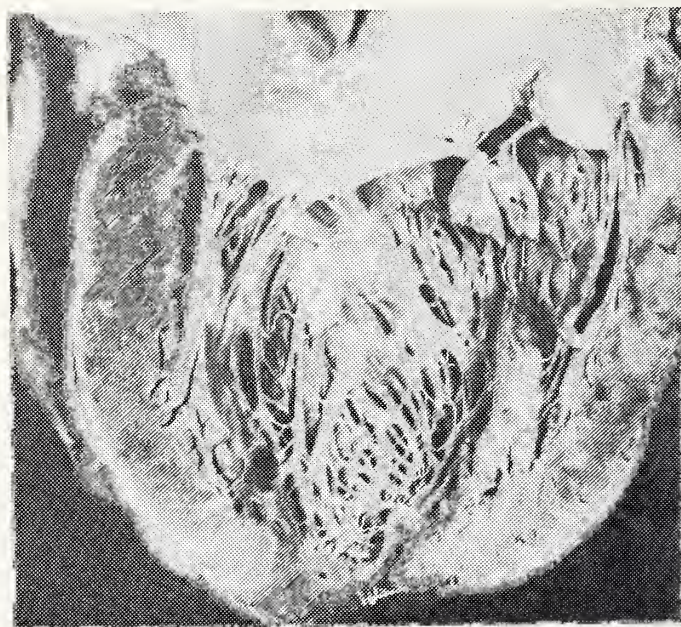


Fig. 17 — Acute myocardial infarction with rupture of posteromedial papillary muscle. As chordae from this muscle extend into each leaflet, the corresponding flail state involves adjacent parts of the anterior and posterior leaflets above the ruptured papillary muscle.



muscle is acute myocardial infarction. If an entire papillary muscle is ruptured, both leaflets lose their support in relation to one commissure, more commonly the posteromedial than the anterolateral commissure. If a limited amount of the units of a papillary muscle ruptures, only part of one leaflet may prolapse.

It is important to distinguish between rupture of chordae and rupture of a papillary muscle as these two conditions potentially have differing echocardiographic signs and underlying causes. When a papillary muscle ruptures, part of the involved papillary muscle is attached to chordae and this structure has the potential for being identified as a moving foreign body within the left-sided cavities.

Also, it is to be recognized that each papillary muscle has chordal connections with each leaflet. Therefore, it is to be expected that rupture of a papillary muscle will yield signs of prolapse of adjacent parts of each leaflet (Figure 17). In contrast, rupture of chordae involves only one leaflet and usually only part of it. Therefore, prolapse from ruptured chordae is expected to be restricted to part of one leaflet.

#### Extraneous Material

Potentially identifiable extraneous material may



Fig. 18 — A portion of the mitral valve showing vegetations of bacterial endocarditis. The latter are deposited upon the contact surfaces of the leaflets.

occur on or in relation to the mitral valve. These include (1) a segment of a ruptured papillary muscle mentioned above (Figure 17), (2) vegetations involving the valve, (3) calcification of the valve and (4) calcification of the valvular annulus.

Vegetations on the mitral valve may be of rheumatic, infectious or non-infectious origins. Vegetations of acute rheumatic fever are uniformly deposited and small. Because of their size, they are probably not detectable by echocardiographic study. Non-bacterial vegetations, as may occur in lupus erythematosus and in wasting diseases (marantic), are more focal and larger than those of acute rheumatic endocarditis. Among the largest vegetations are those of bacterial endocarditis (Figure 18), although in some instances, vegetations of this type are not larger than

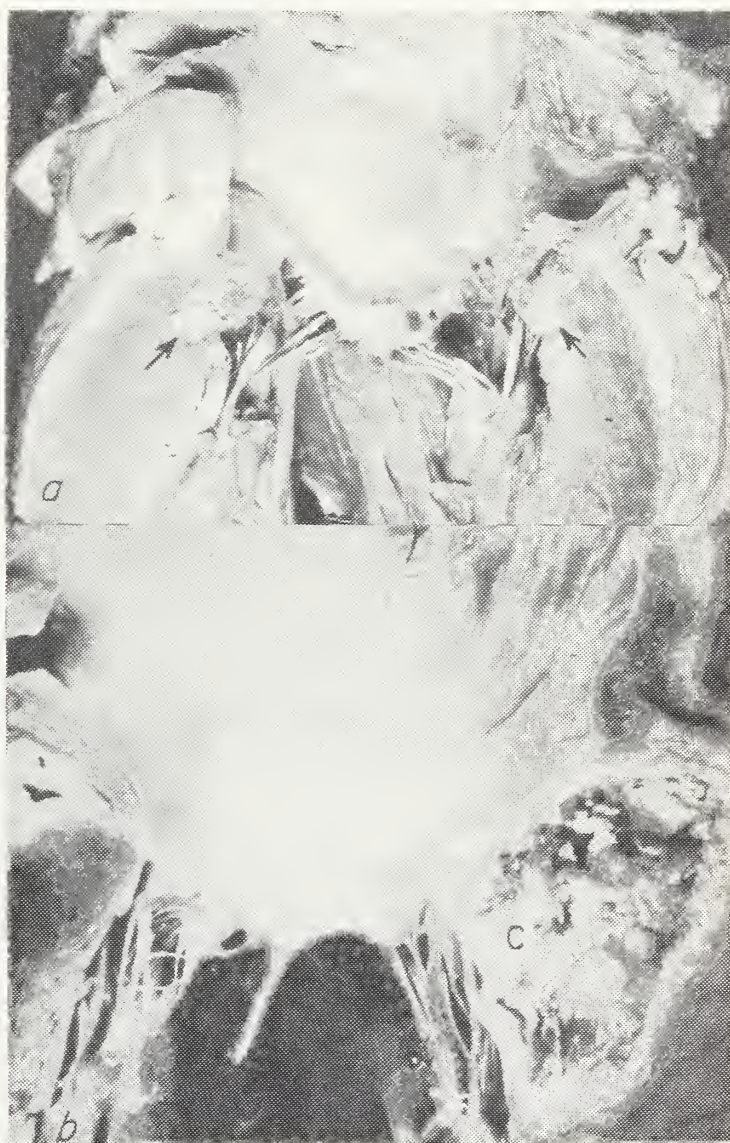


Fig. 19 — Calcification of the mitral ring. (a) The left atrium and left ventricle are exposed showing at the junction of the two structures a calcific mass (arrows) which is adherent to the related posterior mitral leaflet and extending into the substance of the left ventricular wall. (As the dissection was carried through the calcific mass, a portion of it appears in each side of the illustration.) (b) Liquifying calcification of the mitral ring. A large, partly cystic mass (C) lies at the junction of the left atrium and left ventricle.



the range observed in non-bacterial vegetations. Classically, the primary site of deposition of vegetations are on the contact surfaces of the leaflets.

Calcification may involve the mitral leaflets in rheumatic disease.<sup>14,15</sup> Also, in calcific aortic stenosis, a calcific spur may extend into the anterior leaflet.

The most common type of calcification involving the region of the mitral valve is that occurring in the annulus of the valve in relation to the posterior leaflet.<sup>16</sup> This process has been termed "calcification of the mitral ring". While the name might suggest a ring-like structure, it has the shape of a semicircle. The condition is usually seen in the aged and more commonly in the female than in the male. The size of the calcific deposit varies, the larger ones extending into the left ventricular myocardium. Uncommonly, the mass may become adherent to the posterior leaflet (Figure 19(a)) causing the excursion of the latter to be restricted. While the mass is usually solid, it may, at times, be liquified and misinterpreted pathologically as an abscess (Figure 19(b)).

In instances of the floppy mitral valve, calcification may occur in one of several places. Locations included are (1) the basal aspect of the leaflet (Figure 20(a)), (2) the left ventricular mural endocardial thickening in relation to chordae of the posterior leaflet (Figure 20(b)), and (3) chordae (Figure 20(c)).

#### *The Left Atrium*

Enlargement of the left atrium, foreign substances in the chamber and calcification in the left atrial area are potentials for echocardiographic identification.

Left atrial enlargement is usually generalized and secondary either to mitral valvular disease or to atrial fibrillation, the latter either of idiopathic or secondary nature. Rarely, one encounters the entity of a giant left atrial appendage in an otherwise normal heart. Thrombi may form in such an appendage and be a source of systemic embolism.<sup>17</sup>

Foreign substances include thrombi, tumor and the diaphragm of cor triatriatum.

Left atrial thrombi classically have the greatest tendency to occur in the atrial appendage but the process may, in some instances, be more extensive.<sup>18</sup> The latter situation may result either from extension of a thrombus in the appendage protruding into the main part of the cavity or from independent thrombi originating against the atrial wall (Figure 21). At times, particularly in mitral stenosis, such thrombi may occupy a considerable portion of the left atrial space.

Special forms of left atrial thrombosis occur in cases with prosthetic replacement of the mitral valve. In the early postoperative state, flat mural thrombosis may occur in broad distribution on the septal wall. Such thrombi probably result from injury to this area during the operative procedure of valvular replacement. In late postoperative states, thrombi, when present, tend to occur at the inlet to the prosthesis.

Tumors of the left atrium constitute another foreign substance in the left atrium.<sup>19</sup> The most common example is the left atrial myxoma. Classically, this is a solitary tumor, either papillary or smooth-surfaced,

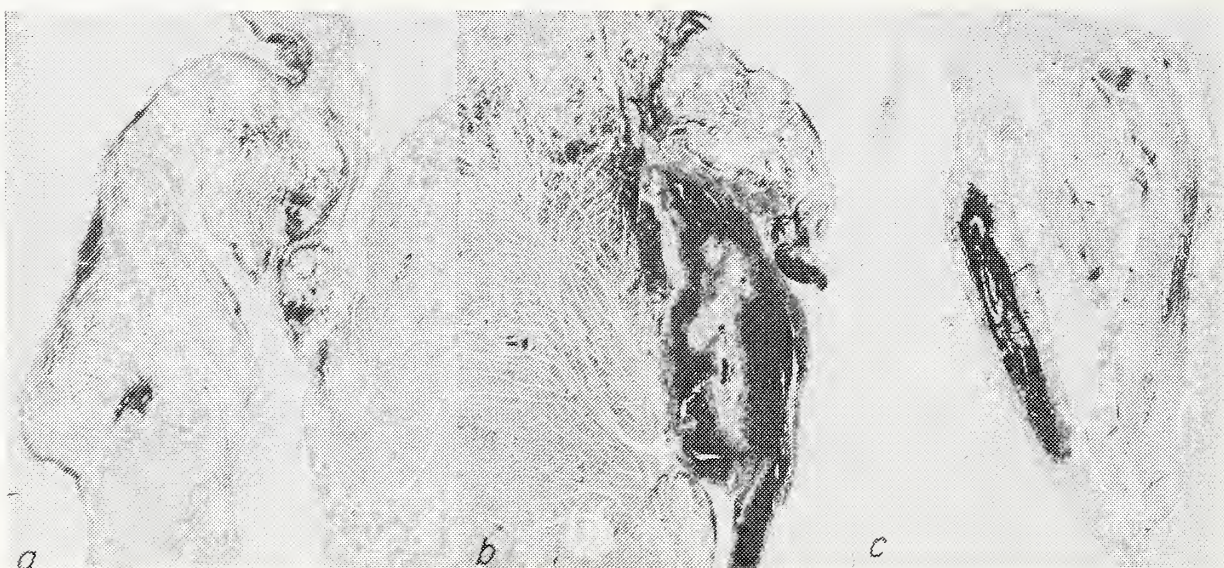


Fig. 20 — Calcification in relation to floppy mitral valve. (a) Low power view of left atrium, left ventricle and posterior mitral leaflet. At the base of the valvular leaflet and at the annulus is a focus of calcification. The leaflet shows distension by myxomatous change. H & E; x 4. (b) Junction of left atrium, left ventricle and posterior mitral leaflet with a friction lesion of the endocardium of the left ventricle. The pale material at the center of the thickened mural endocardium represents calcification. Elastic tissue; x 4. (c) Chordae attaching to the anterior mitral leaflet. One of the chordae shows a large focus of heavy calcification. H & E; x 4.



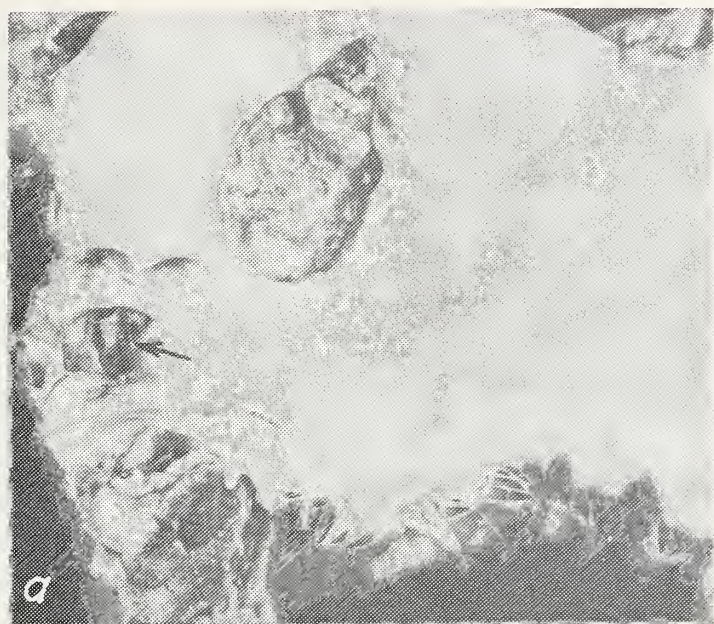


Fig. 21 — Left atrial thrombosis. (a) Attached to the septal wall of the left atrium is a pedunculated mural thrombus in a case of old myocardial infarction with congestive heart failure. Thrombosis is also present in the appendage (arrow). (b) Left atrium and left ventricle in a case of mitral stenosis. The left atrium contains a large thrombus which occupies considerable space in the atrium. At the right upper part of the illustration the reflected wall of the left atrium shows residual thrombus attached to it.

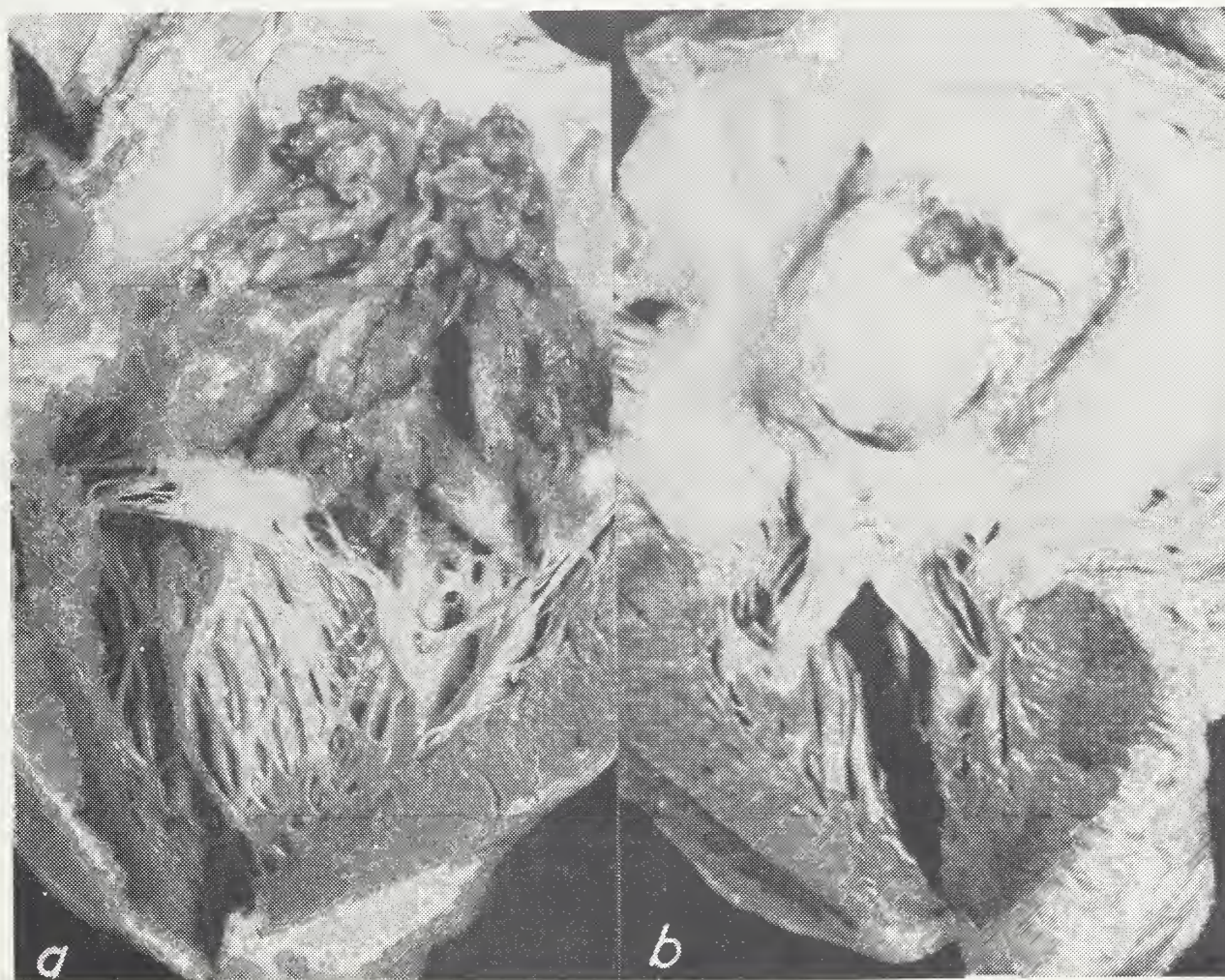


Fig. 22 — Left atrial myxomas. (a) A pedunculated and lobulated tumor is attached to the septal wall of the left atrium and approaches the mitral valve. (b) A calcified left atrial myxoma with smooth surface. There is secondary fibrosis of the mitral leaflets and chordae, while the commissures are not fused. (From Carter et al.: *Am J Cardiol* 33:914, 1972; with permission.)



that is attached by a pedicle to the septal wall (Figures 22 and 23). Initially, the tumor is not calcified but may become so with time (Figure 22(b)). Being attached by a pedicle, the tumor moves in concert with the changing forces through the cardiac cycle and may engage the mitral orifice during ventricular diastole. This process may injure the mitral valve leaflets and chordae resulting in fibrosis of these structures (Figure 22(b)).<sup>20</sup>

In the congenital condition, cor triatriatum, the left atrium is divided by a perforated diaphragm into two segments, an upper, receiving the pulmonary veins, and a lower, connecting with the mitral valve and the atrial appendage (Figure 24). The dividing membrane has the potential for echocardiographic detection.

Localized calcification in relation to the left atrium may be that of a calcified myxoma or a calcified old thrombus. Unusually, and particularly in mitral stenosis, there may be extensive calcification of the left atrial wall.<sup>21</sup>

#### *The Aortic Root*

Variations occur at the aortic root both in diameter of the lumen and in thickness of the wall.

Extreme narrowing of the ascending aorta including the root of the aorta occurs in neonates with aortic valvular atresia.

Progressive widening of the lumen of the aorta with age is a normal phenomenon. Clear examples of widening are commonly seen in subjects in the ninth decade and older. Aortitis, sometimes seen with calcification of the aortic wall, is yet another cause of dilatation of the aortic root.

Extreme degrees of diffuse widening of the aortic root are observed in individuals with extensive cystic medial necrosis of the aorta (Figure 25).<sup>22</sup> Some of such subjects exhibit the physical characteristics of arachnodactyly (Marfan's syndrome).

Localized dilatation of the right side of the ascending aorta is seen in aortic valvular stenosis as the phenomenon of poststenotic dilatation.

Those examples of dissecting aneurysm of the aorta in which the internal tear lies in the ascending aorta shows not only widening of the outer diameter of the vessel but thickening of its wall. The latter represents the intramural hematoma characteristic of this condition (Figure 26).<sup>23</sup> In individuals who have survived for months or years following the initial event of dissecting aortic aneurysm, the walls of the false passage may become calcified.

#### **The Aortic Valve**

The cusps of the aortic valve are subject to restricted



Fig. 23 — View from above of the opened left atrium showing a pedicle (arrow) by which a left atrial myxoma is attached to the septal wall. A thrombus is also attached to the right side of the myxoma.



Fig. 24 — Cor triatriatum. The left atrium is divided into two segments, an upper (T) with which the pulmonary veins connected, and a lower chamber (LA), which is in communication with the left atrial appendage (LAA) and the mitral valve. The probe is in the perforation of the diaphragm that separates the two cavities of the left atrium. LV = left ventricle. (From Lucas et al.: *Ped Clin No Amer* 10:781, 1963; with permission.)



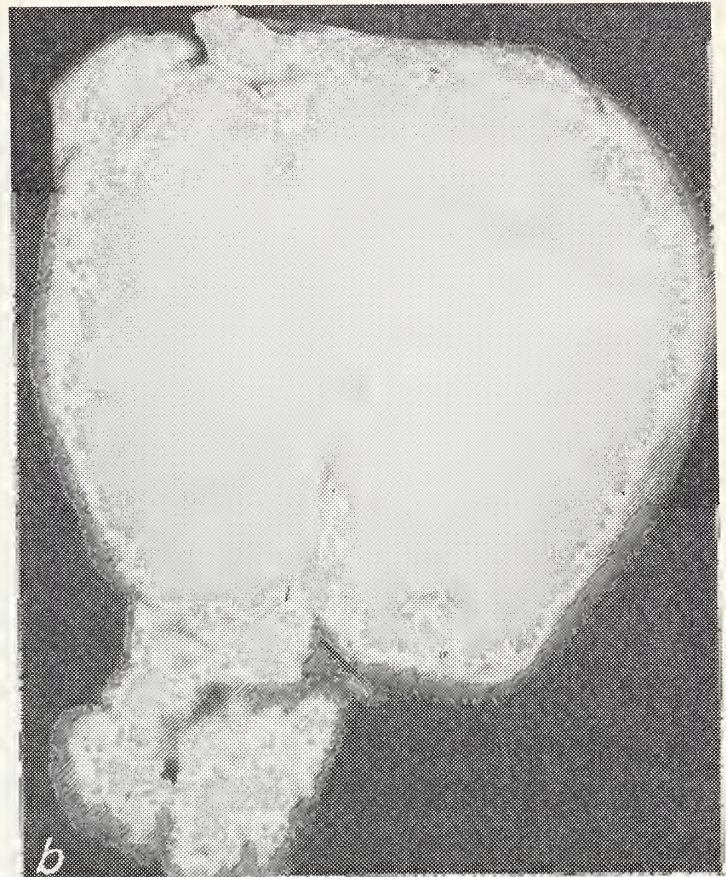
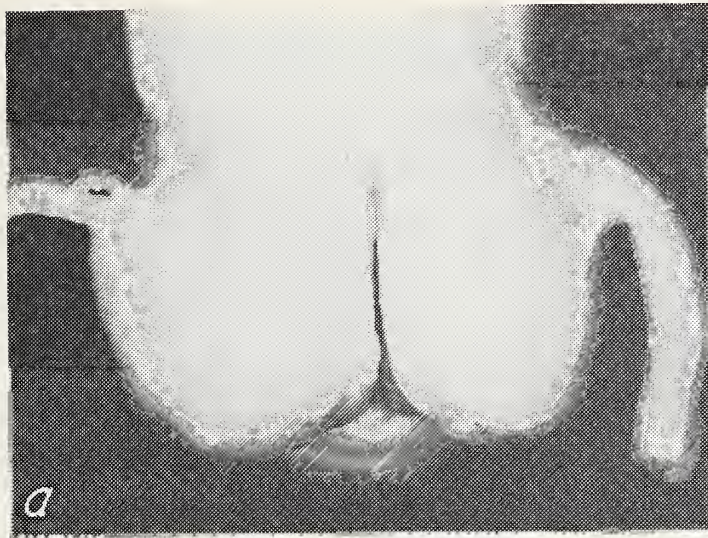


Fig. 25 — Comparison of casts of aortic root from (a) the normal and (b) from a case of extensive cystic medial necrosis in an individual with arachnodactyly (Marfan's syndrome). In (b) the mass extending below the cast of the dilated aortic sinuses represents injected material which has regurgitated through the incompetent aortic valve.

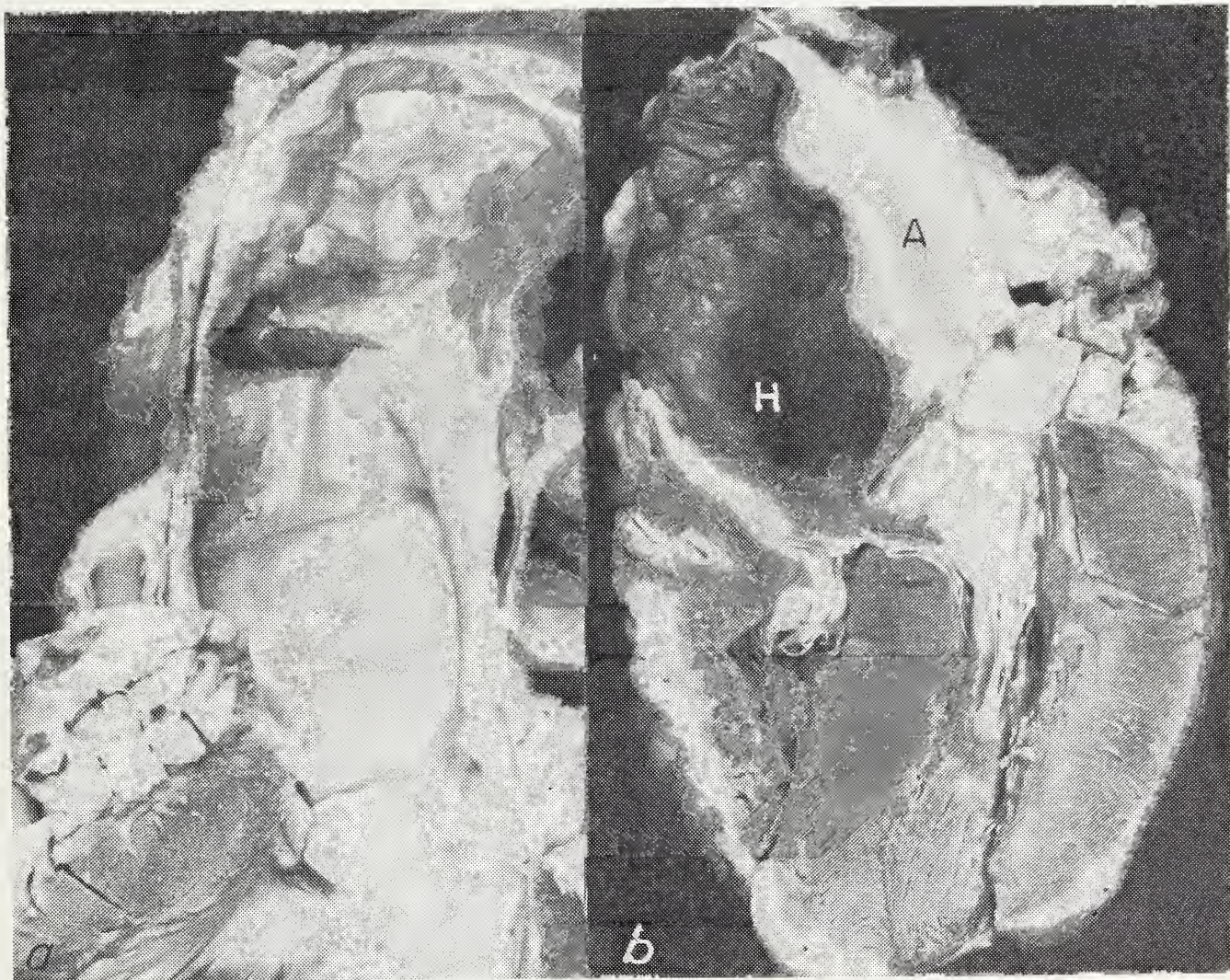


Fig. 26 — Dissecting aneurysm of the aorta. (a) The interior of the ascending aorta, within which there is a laceration leading into a false passage. (b) Longitudinal section through the ascending aorta, the false passage (H), true lumen of the aorta (A) and the heart. The false passage adds to the external width of the ascending aorta.



motion, prolapse and sites for deposit of foreign material.

#### *Restricted Motion*

Restricted motion of the cusps may either be congenital or acquired. The latter may result from commissural fusion or from intrinsic calcification of cuspid tissue.

A congenital basis for restriction of motion of aortic cuspid tissue may be fusion of the valvular tissue to form aortic valvular atresia. The condition characteristically is associated with a hypoplastic aorta. It is usually observed in the newborn, as aortic atresia has a great tendency to be lethal during the first week of life. The deformity of congenital aortic valvular stenosis may allow subjects to reach adult life. In this state, there is but one commissure and the valve takes the form of a modified dome (the so-called unicommissural, unicuspid aortic valve).<sup>24</sup>

In subjects born with three cusps, restriction of cuspid motion may result from rheumatic disease with fusion of one or more commissures. Fusion of but one commissure yields an acquired bicuspid valve (Figure 27(a)).<sup>25</sup> If two or more commissures are fused, aortic stenosis usually results, even in the absence of valvular calcification (Figure 27(b)).

Calcification of cusps may be of varying degree and with varying backgrounds. It is a common phenomenon that in the sixth decade of life alteration begins in the connective tissues of bases of the cusps of normal aortic valves and related free wall. These alterations lead to calcification. In most instances, the degree of

calcification is inadequate to restrict cuspid motion significantly and aortic stenosis does not result.

In exceptional cases, the distribution of calcium in the cusps is so extensive that without commissural fusion, stenosis results (Figure 28(a)). The process may be termed the senile type of calcific aortic stenosis. More common as a type of calcific aortic stenosis is that resulting from calcification of either a congenital (Figure 28(b)) or an acquired bicuspid aortic valve (Figure 28(c)). Less commonly, extensive calcification occurs in a congenitally unicuspid aortic valve (Figure 28(d)).

#### *Prolapse*

Prolapse of one or more aortic cusps may result from inadequate support of a leaflet.<sup>26</sup> This may come about from loss of continuity of the substance of a cusp as from bacterial endocarditis or external non-penetrating trauma. Loss of support of cusps may also result from a laceration of the ascending aorta, either from blunt trauma to the chest or spontaneously. If the laceration is positioned in relation to a commissure of the valve, the flail state of the aortic wall in relation to the laceration allows the related commissure and cusps to prolapse (Figure 29).<sup>26</sup>

#### *Foreign Material*

Deposits of foreign material upon or in aortic cusps include calcific deposits in the cusps (see above) and the presence of vegetations upon the contact surfaces. The most likely basis for a vegetation to be sufficiently large as to be detected echocardiographically is

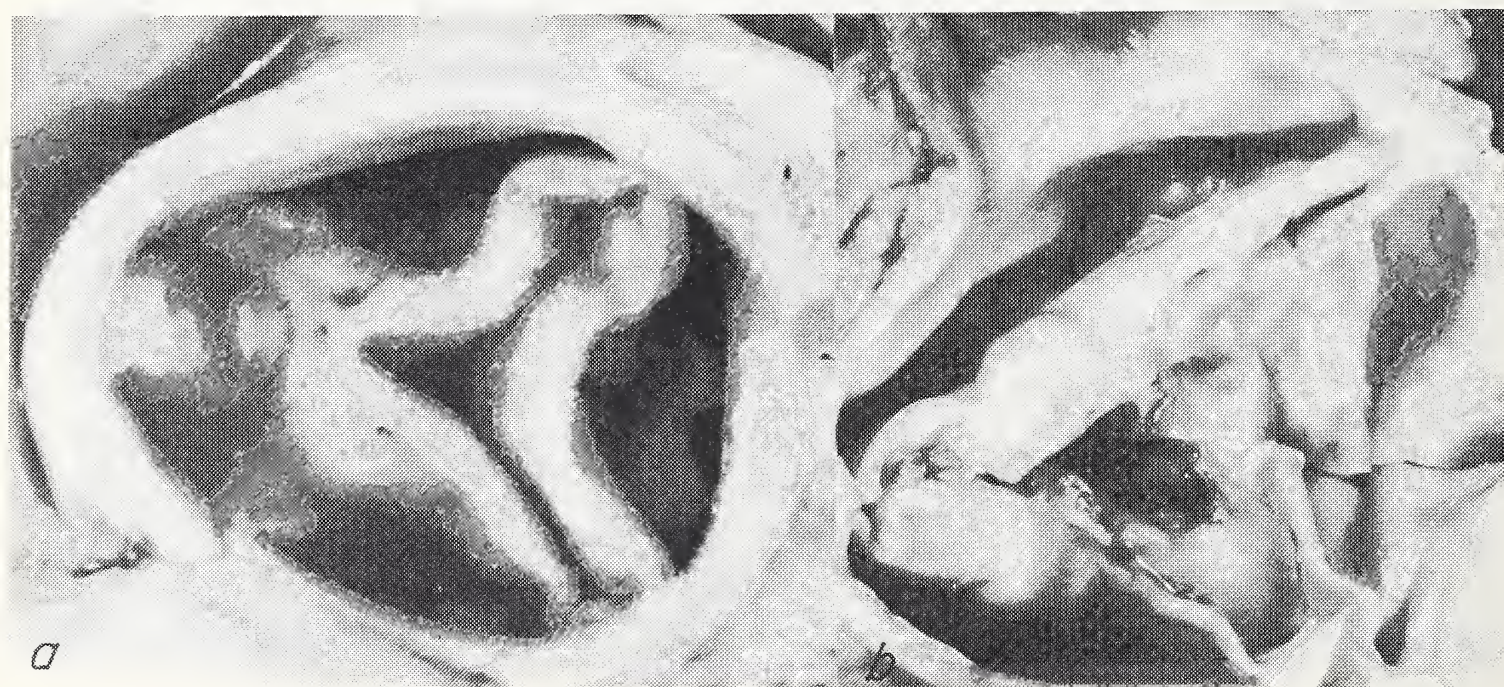


Fig. 27 — Rheumatic aortic valvulitis. (a) Fusion of two of the cusps at a commissure, yielding an acquired bicuspid aortic valve. (b) Fusion at two commissures along with marked thickening of the cusps leads to aortic stenosis.



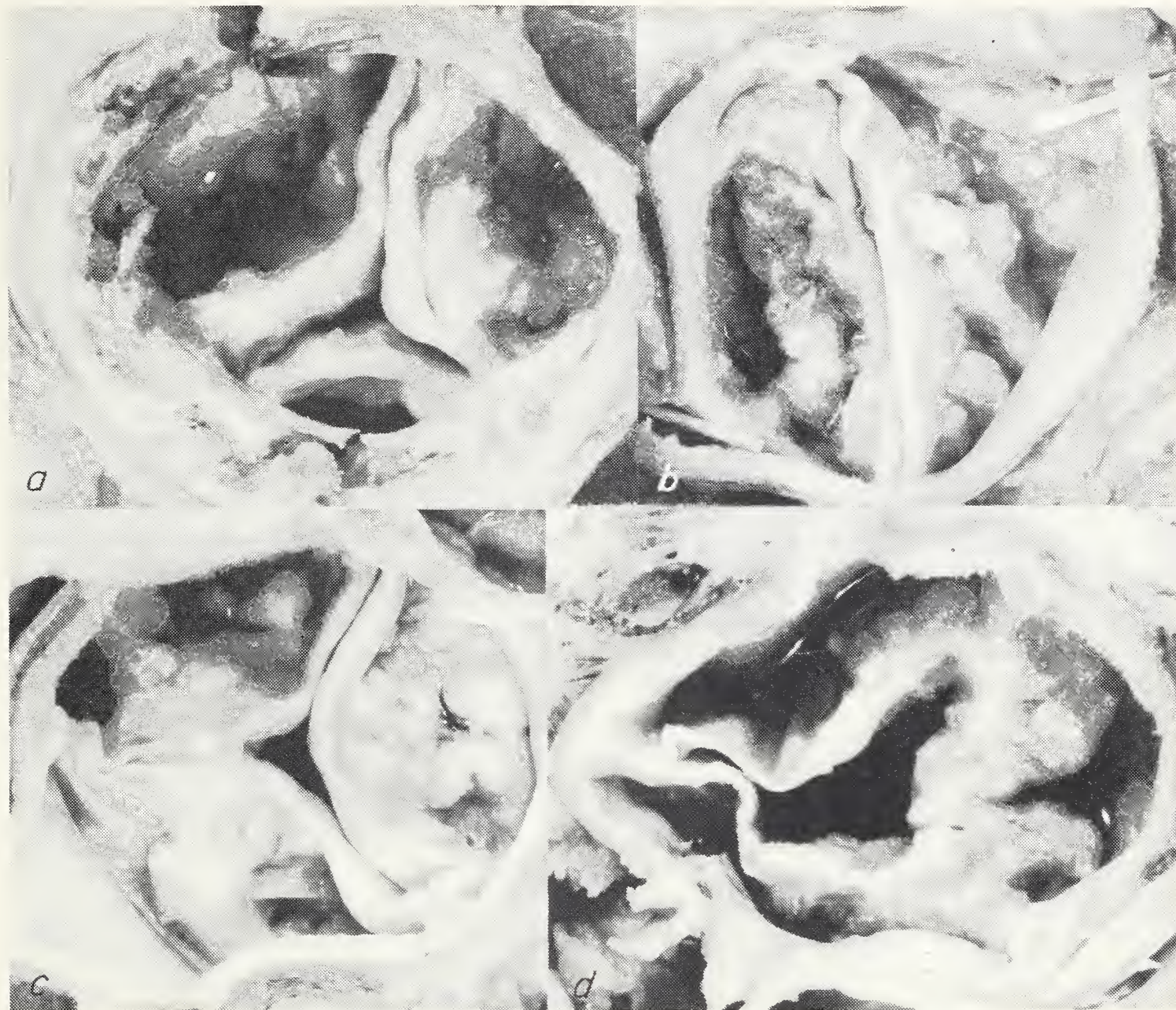


Fig. 28 — Varieties of calcific aortic stenosis. In each instance the unopened aortic valve is viewed from above. (a) Senile calcific aortic stenosis. There are three cusps and the commissures are not fused. (b) Congenital bicuspid aortic valve with secondary calcification. (c) Acquired bicuspid aortic valve with secondary calcification. (d) Unicuspid, unicommisural aortic valve with calcification.

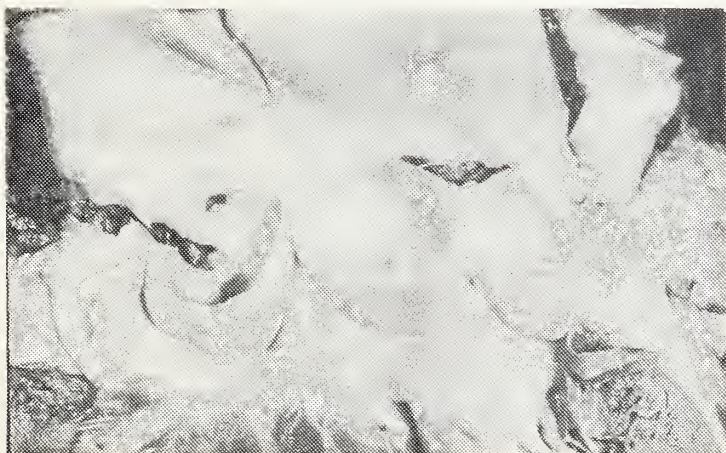


Fig. 29 — Traumatic lacerations of the ascending aorta in relation to aortic commissures. The flail state of the aortic wall in relation to the lacerations allows for commissural prolapse and aortic insufficiency.





Fig. 30 — Left ventricle and congenital bicuspid aortic valve. A vegetation of bacterial endocarditis is deposited upon the aortic valve.

infective endocarditis (Figure 30).

### Summary

As a background for echocardiographic study of the heart, an anatomic review is presented. This includes highlights of the normal structure. Consideration is given to those alterations in the pericardium, the chambers, the left-sided valves and the aortic root that have the potential for echocardiographic identification.

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# Role of Echocardiography in Emergencies

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The use of echocardiography in urgent or emergent clinical situations is reviewed. In general echocardiography is of value in detecting lesions which cause obstruction to blood flow or acute anatomical cardiac abnormalities. Examples of the utility of echocardiography in such clinical situations are presented.

**E**CHOCARDIOGRAPHY PROVIDES a unique method of imaging cardiac structures. It follows that M-mode echocardiography should be of benefit in certain urgent or emergent clinical situations and that in selected clinical situations it may be the diagnostic procedure of choice. In our experience echocardiography has been helpful in establishing the correct diagnosis when cardiac tamponade, intracardiac tumor, prosthetic mitral valve dysfunction, aortic root dissection, or acute valvular abnormalities are suspected.

## Cardiac Tamponade

Although cardiac tamponade is a clinical diagnosis,

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certain echocardiographic features may lead to the correct diagnosis of this cause of obstruction to blood flow. If the clinical findings are diagnostic or the patient is in imminent danger, pericardiocentesis should be done promptly, since echocardiography will only provide supplementary information. Figure 1 is an echocardiogram taken on a 65 year old female with metastatic breast carcinoma who presented with lethargy and hypotension. An echo-free zone anterior to the right ventricular free wall and posterior to the left ventricular posterior wall indicates the presence of a pericardial effusion. In addition, the heart is noted to be "swinging" in the effusion with two alternating positions relative to the anterior chest wall<sup>1</sup> (Figure 1). Electrical alternans is noted on the simultaneously recorded electrocardiogram, with the higher amplitude QRS complexes corresponding with the closer position

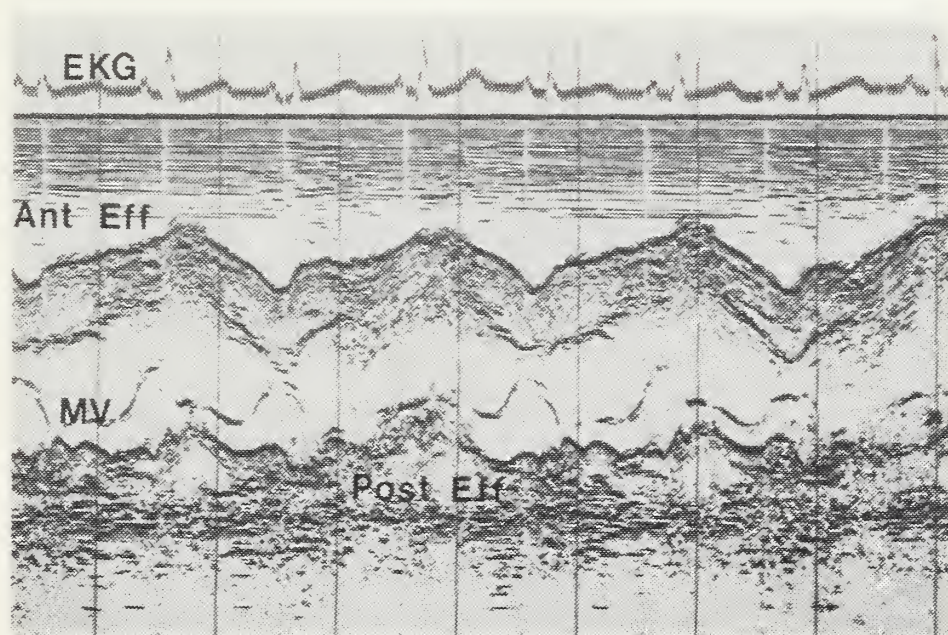


Fig. 1 — Echogram from 65 year old female with metastatic breast carcinoma. Ant. Eff. = Anterior Pericardial Effusion. Post. Eff. = Posterior Pericardial Effusion. MV = Mitral Valve. Note the heart is "swinging" in a large pericardial effusion with two alternating positions relative to the anterior chest wall. Electrical alternans is present with higher amplitude QRS complexes corresponding with the closer position of the heart to the anterior chest wall.



of the heart to the anterior chest wall. Pulsus paradoxus was also present, and a pericardiocentesis was done, with removal of 300 cc of bloody fluid from the pericardial cavity. An echocardiogram taken immediately after the tap (Figure 2) demonstrates a small pericardial effusion and a large pleural effusion but no evidence for a "swinging heart". The "swinging heart" abnormality of cardiac motion may be present with large effusions with or without clinical findings of tamponade; nevertheless it should alert the clinician to the potential of cardiac tamponade.<sup>2</sup>

The relative filling volumes of the right and left ventricle during the respiratory cycle have been incriminated in the mechanism of pulsus alternans.<sup>3,4</sup> Figure 3 depicts an echocardiogram from a 63 year old male with known metastatic squamous cell carcinoma

of the lung. Pulsus paradoxus was present but electrical alternans was absent. Right and left ventricular dimensions as well as mitral valve motion are shown for several respiratory cycles. The end-diastolic dimension of the right ventricle is markedly decreased at end-expiration, while mitral valve diastolic excursion and the D-E slope are increased. These features are consistent with decreased right ventricular filling and increased left ventricular filling at end-expiration. Reciprocal changes occur during inspiration. These findings have been described as reliable echocardiographic indicators of cardiac tamponade by Schiller et al.<sup>4</sup> Figure 4 demonstrates an echocardiogram of the same patient taken after pericardiocentesis. A pericardial effusion is still present, but there are no respiratory changes in chamber dimension or valvular motion

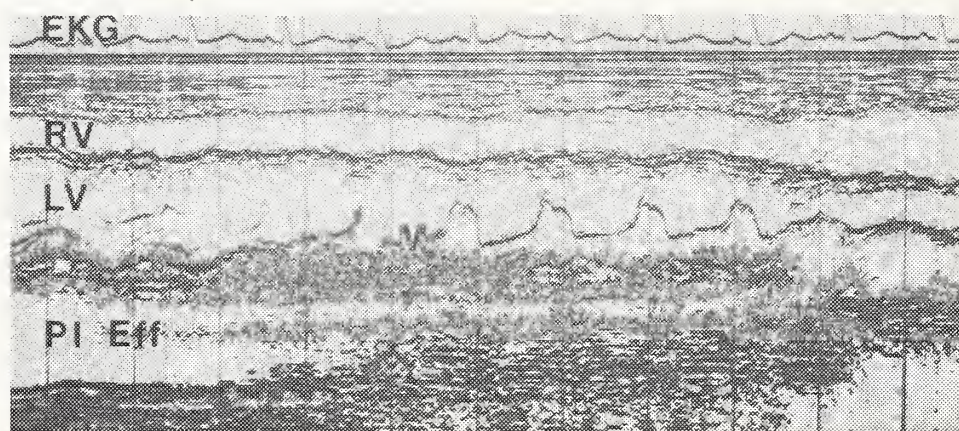


Fig. 2 — Echogram from same patient as shown in Figure 1, taken immediately following removal of 300 cc of fluid by pericardiocentesis. RV = Right Ventricular cavity. LV = Left Ventricular cavity. M = Mitral Valve. PI. Eff. = Pleural Effusion. Black arrow indicates pericardial effusion. Evidence of "swinging heart" or electrical alternans is no longer present.

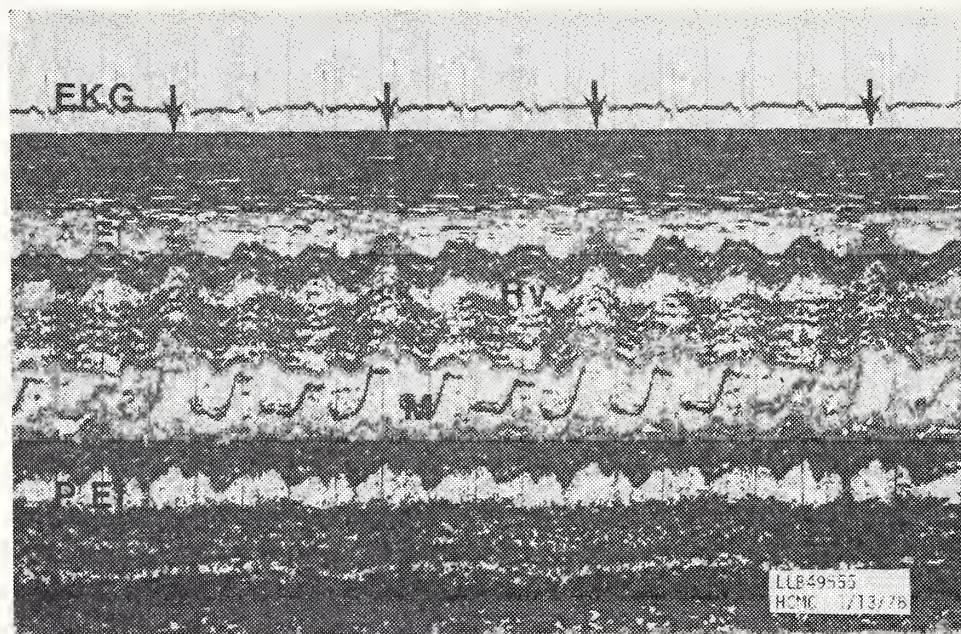


Fig. 3 — Echogram from 63-year-old male with metastatic lung carcinoma. A. Ef. = Anterior Pericardial Effusion. P. Ef. = Posterior Pericardial Effusion. RV = Right Ventricular Cavity. M = Mitral Valve. End expiration is indicated by black arrows. Note the decreased RV dimension and increased mitral valve diastolic excursion and D-E slope at end-expiration. Reciprocal changes in RV dimension and mitral valve motion are noted during inspiration.



detectable.

### Intracardiac Tumors

The efficacy of echocardiography in the detection of intracardiac tumors is well established. The clinical presentations of patients with intracardiac tumors is variable and symptoms and signs secondary to obstruction of blood flow may occur.<sup>5,6</sup> The following

case is a dramatic example of obstruction of blood flow secondary to a left atrial myxoma, in which the diagnosis was established by echocardiography. The patient was a 55-year-old man who presented with lethargy and anasarca. Carotid and femoral pulses were present but no blood pressure was audible by the cuff method and his neck veins were markedly distended. An echocardiogram was obtained to rule out

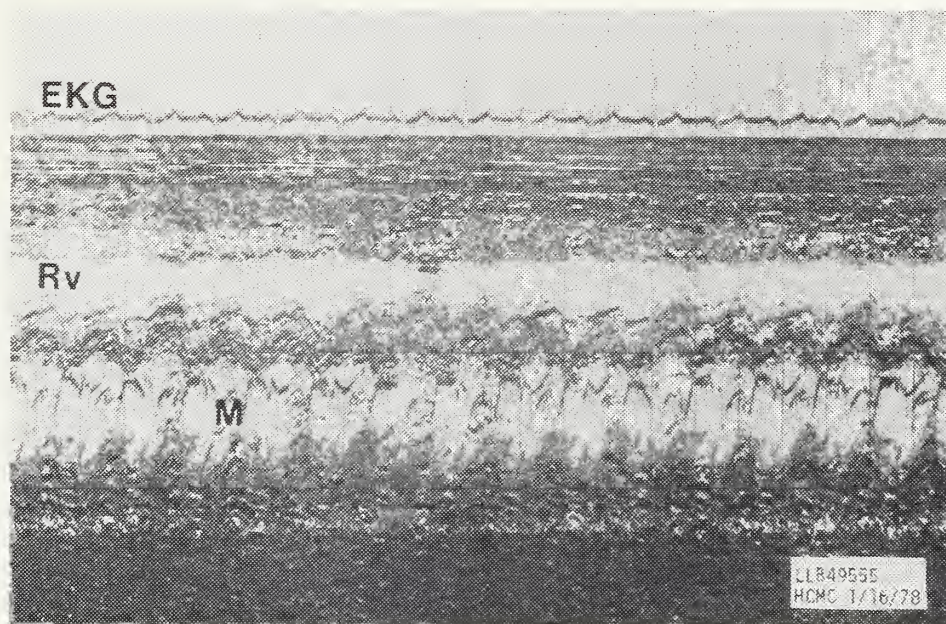


Fig. 4 — Echocardiogram from the same patient shown in Figure #3, taken during normal respiration after pericardiocentesis. RV = Right Ventricular Cavity. M = Mitral Valve. Note the absence of any changes in right ventricular cavity dimension or mitral valve motion during normal respiration.

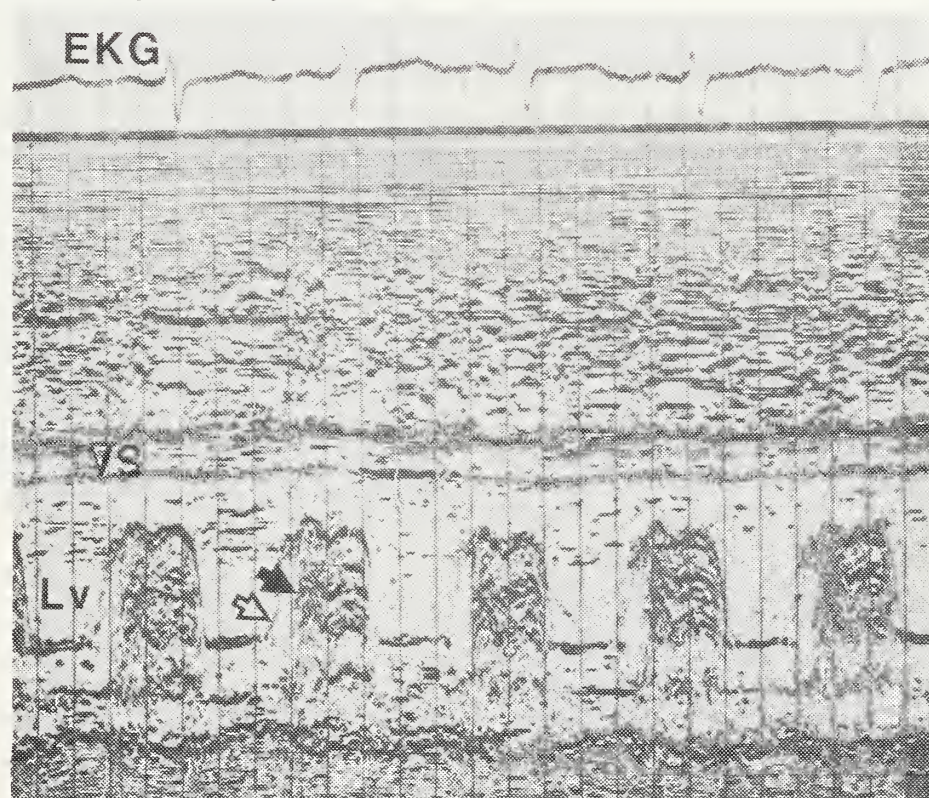


Fig. 5 — Echocardiogram from 55-year-old male with left atrial myxoma causing obstruction to blood flow at mitral valve level. IVS = Interventricular Septum. Lv = Left Ventricular Cavity. Open arrow indicates the anterior mitral valve leaflet in early diastole. Closed arrow indicates prolapsing left atrial myxoma. Note the clear space between the anterior mitral valve leaflet and prolapsing myxoma.<sup>7</sup>



a pericardial effusion and instead the diagnostic pattern of a left atrial myxoma was found (Figure 5). A large mass of echoes is seen posterior to the anterior mitral valve leaflet in diastole. A clear space between the opening of the mitral valve and the prolapsing left atrial myxoma is present.<sup>7</sup> This patient was taken directly to the operating room on the basis of the clinical and echocardiographic findings. The tumor was successfully removed and a complete recovery was eventually made.

### Prosthetic Mitral Valve Evaluation

The ability to image prosthetic valves and the all-too-frequent occurrence of malfunction of prosthetic valves has led to studies concerning the use of echocardiography in detecting malfunction of prosthetic valves. Simultaneous echocardiography and phonocardiography can be utilized to determine the interval from the aortic component of the second heart sound to the mitral valve opening (*A2-MVO interval*) (Figure 6). A decrease in the A2-MVO interval may occur if left atrial pressure at end-systole is elevated secondary either to obstruction at mitral valve level or to insufficiency across the mitral valve with a large c-v pressure wave in the left atrium.<sup>8</sup> It is important, however, to note that the A2-MVO interval is dependent upon three factors: (1) Aortic pressure at the time of the aortic component of the second heart sound; (2) Left atrial pressure at the left ventricular-left atrial pressure crossover point; and (3) The rate of decline of left ventricular pressure during isovolumic relaxation.

Although interpretation of the A2-MVO interval must be made with regard to these three variables, the A2-MVO interval may be of clinical value if baseline

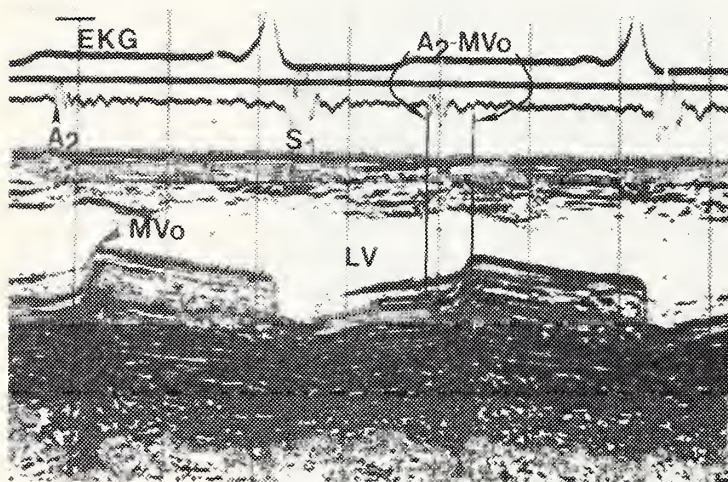


Fig. 6 — Echocardiogram from 29 year old female with normally functioning tilting disc prosthesis (Bjork-Shiley). S<sub>1</sub> = 1st heart sound. A<sub>2</sub> = Aortic component of second heart sound. LV = Left Ventricular Cavity. MVO = Opening of Prosthetic Mitral Valve. A<sub>2</sub> - MVO = Interval from the aortic component of the second heart sound to the opening of the mitral valve.

and follow-up studies are obtained on individual patients so that meaningful comparisons are available.

The *diastolic motion of the posterior wall of the aorta* has also been utilized for indirect analysis of obstruction at mitral valve level. It must be remembered that the posterior wall of the aorta is contiguous with the anterior wall of the left atrium. Diastolic left atrial emptying is noted by posterior motion of the posterior aortic wall. Three phases of left atrial emptying are defined when no obstruction is present at the mitral valve<sup>9</sup> (Figure 7, Panel B). These include: (1) a rapid emptying phase; (2) a left atrial 'conduit'

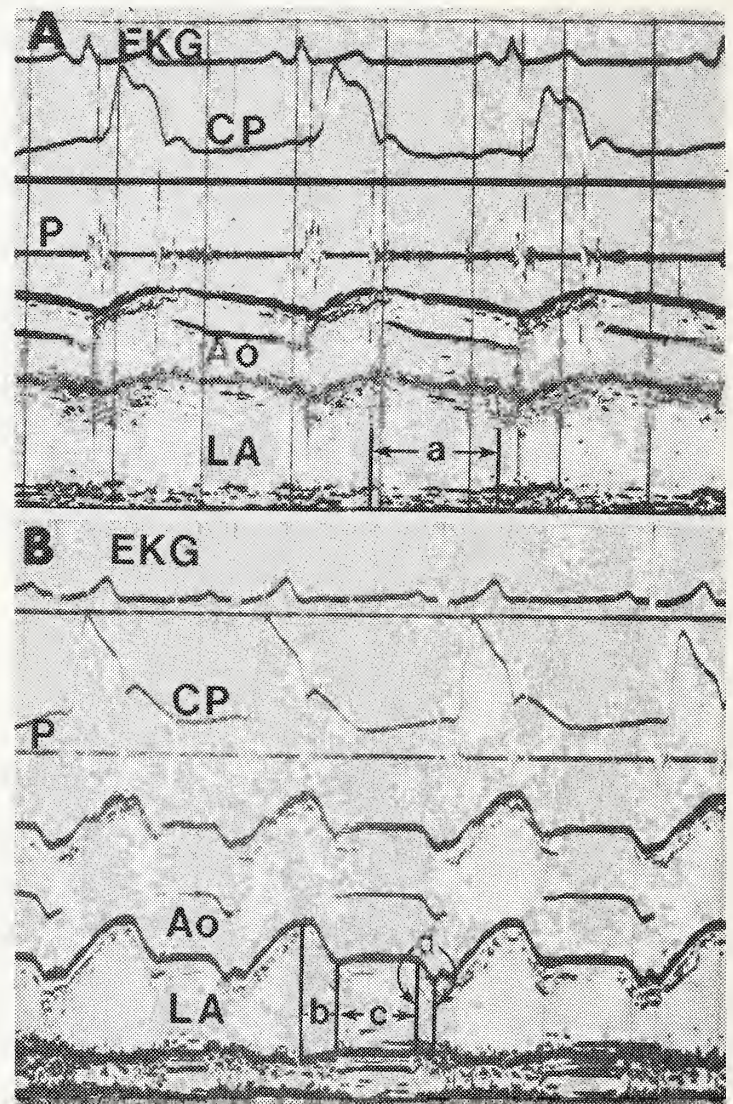


Fig. 7 — Panel A: Echocardiogram from a 24-year-old female with isolated mitral stenosis (mitral valve area was 1.1 cm<sup>2</sup> at cardiac catheterization). CP = External Carotid Pulse Tracing, P = Apex Phonocardiogram, Ao = Aortic Root, and LA = Left Atrium. The dimension of the left atrium during diastole (noted by -a-) gradually decreases without discernible rapid emptying in early diastole or notable decrease in dimension subsequent to atrial systole.

Panel B: Echocardiogram from a normal healthy 25-year-old male. CP, P, Ao, & LA as in Panel A. The three normal diastolic phases of left atrial emptying are apparent: b-rapid emptying in early diastole, c - diastasis or atrial conduit phase, and d - atrial emptying subsequent to atrial systole but preceding the QRS complex. Note the differences between this echo and that in Panel A.



phase; and (3) left atrial emptying secondary to atrial systole. When obstruction occurs at the mitral valve level as in mitral stenosis (Figure 7, Panel A) or with malfunction across a prosthetic mitral valve, there is a decrease in the rate of rapid emptying, with a rather constant decrease in left atrial dimension throughout diastole (Figure 7, Panel A). Quantitative indices derived from the diastolic motion of the posterior aortic wall have been used to detect prosthetic mitral valve dysfunction.<sup>9</sup> Many factors could limit the clinical usefulness of these indices. These factors include: left atrial size and shape; initial left ventricular diastolic pressure; total and forward left ventricular stroke

volume; the left ventricular pressure-volume relationship; and pulmonary artery pressure. However, serial studies of individual patients can be of considerable clinical value in detecting prosthetic mitral valve dysfunction. A particular advantage of this method for detecting obstruction at mitral valve level is that it is not dependent upon imaging the prosthesis itself.

### Aortic Dissection

Although the following abnormalities may be useful in leading to the correct diagnosis of aortic dissection, they are not diagnostic and hence the echocardiogram is not a substitute for angiography. Furthermore, aortic

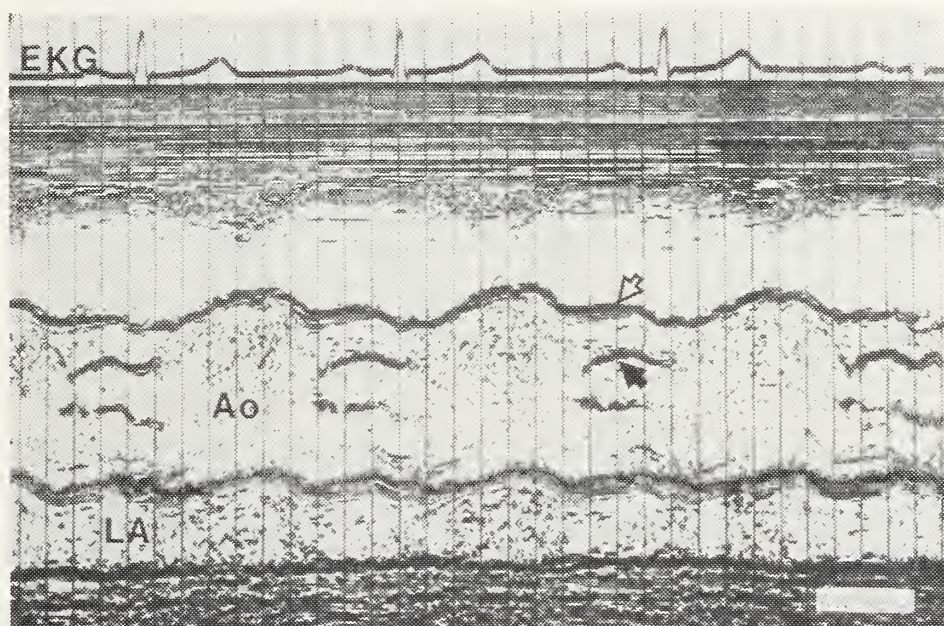


Fig. 8 — Echogram from 46-year-old male with acute aortic root dissection. Ao = Aortic Root. LA = Left Atrium. Open arrow indicates the outer surface of the anterior aortic wall. Closed arrow indicates the inner surface of the anterior aortic wall. The anterior wall of the proximal aorta is 12 mm thick and is consistent with dissecting hematoma.

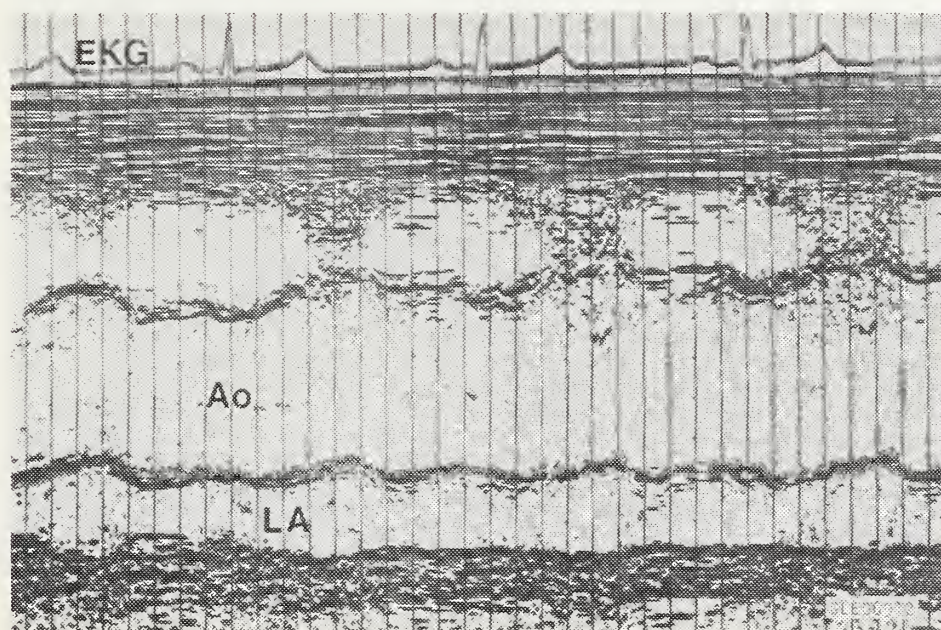


Fig. 9 — Echogram of aorta above aortic valve level from the same patient noted in Figure #8. Ao = Aorta above aortic valve level. LA = Left Atrium. Dilatation of the proximal aorta to 52 mm is noted.



dissection may occur in the absence of the following abnormalities. Acute dissection of the proximal aorta should be considered, however, when the following clinical and echocardiographic features are all present:<sup>10</sup>

(1) An aortic root dimension greater than 42 mm; (2) Increased thickness of the anterior and/or posterior wall of the aorta, particularly if the anterior aortic wall thickness exceeds 15 mm; (3) Parallel motion between the inner and outer margins of the anterior and/or posterior aortic wall; (4) and, perhaps most important, a clinical setting which is consistent with the diagnosis of acute aortic dissection.

Figures 8 and 9 depict echocardiograms of the aortic root from a 46-year-old man who presented with acute onset of anterior chest pain with radiation to the interscapular area. No murmurs were present on arrival in the emergency room, but examination on admission to the Coronary Care Unit one hour later demonstrated a Grade II/VI diastolic blowing murmur at the left sternal border. In addition, a discrepancy of 40 mmHg between right and left brachial artery pressures by the cuff method was noted and the chest x-ray demonstrated mediastinal widening. An echocardiogram of the proximal aorta (Figure 8) demonstrated a double anterior wall echo present in systole indicating a wall thickness of 12 mm. Figure 9 depicts the aorta above aortic valve level and demonstrates marked dilatation of the aorta to a dimension of 52 mm. This patient was taken to surgery

on the basis of these clinical and echocardiographic findings. An acute dissection was present and a complete resection of the proximal aorta and aortic valve was performed with replacement by a composite aortic graft.<sup>11</sup>

### Acute Valve Abnormalities

#### Mitral Valve

Acute abnormalities in the supporting structure of the mitral valve can also be detected echocardiographically. The echocardiogram in Figure 10 is from a 60 year old man who presented with shortness of breath and a new apical holosystolic murmur. The echo demonstrates the features of ruptured chordae tendineae with a flail posterior mitral valve leaflet.<sup>12,13,14,15</sup> There is anterior diastolic motion and posterior systolic motion of the posterior mitral valve leaflet. In addition, there are irregular, inconsistent diastolic echos from the mitral valve. These features have been described with flail posterior mitral valve leaflets secondary to ruptured chordae tendineae; however, we have no further documentation in this patient since he refused further investigation. Figure 11 depicts the echocardiogram at the mitral valve level from a 67-year-old man hospitalized with an acute inferior myocardial infarction who suddenly developed pulmonary edema and cardiogenic shock. Mitral valve motion is markedly abnormal, with wide excursions and irregular motion of the mitral valve in both systole and diastole. Angiography demonstrated

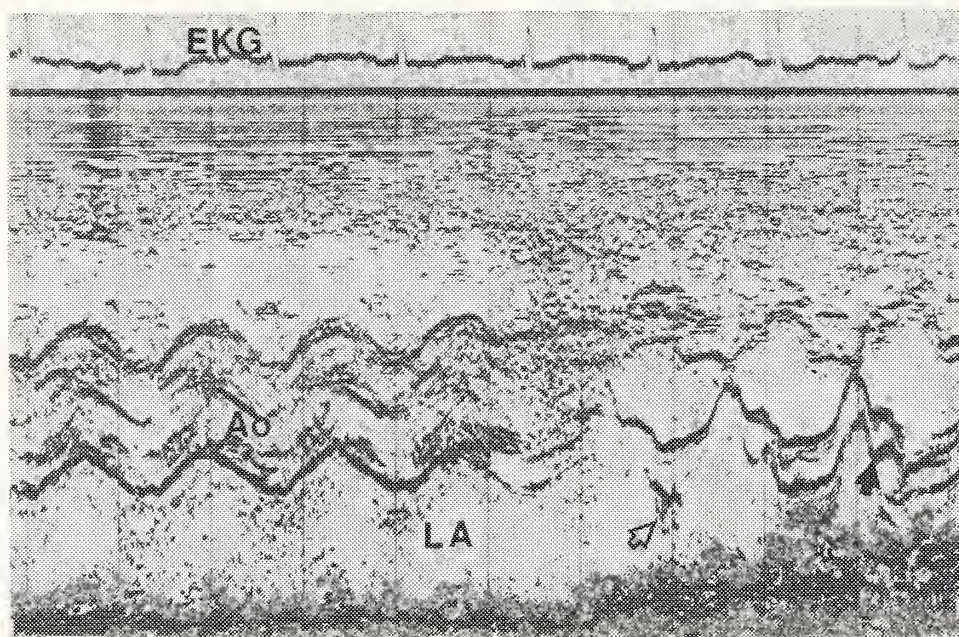


Fig. 10 — Echogram from 60 year old male with clinical findings for a recent onset of mitral insufficiency. Ao = Aortic Root, LA = Left Atrium. Markedly abnormal posterior mitral valve motion is present. In systole the posterior mitral valve leaflet demonstrates multiple echoes with posterior motion into the left atrium (open arrows). In diastole, the posterior mitral valve leaflet (closed arrow) parallels motion of the anterior mitral leaflet.



severe mitral regurgitation with evidence of a ruptured papillary muscle which was confirmed at the time of surgery.

Vegetative lesions associated with mitral valve endocarditis may also be imaged.<sup>16</sup> Typically these vegetations have an increased echo density with a shaggy appearance on M-mode echocardiography. A typical example is noted in Figure 12 which is an echo from a 15-year-old male who presented with chills, fever, and evidence of acute embolism to the right femoral artery. Typical shaggy dense echoes associated with the posterior mitral valve leaflet are seen.

Surgical intervention two days later confirmed a vegetation on the posterior mitral valve leaflet.

#### *Aortic Valve*

The echocardiogram noted in Figure 13 demonstrates the area of the left ventricular outflow tract in a 52-year-old woman on chronic hemodialysis who had presented with chills and fever and evidence of systemic emboli. Blood cultures were positive for gram positive staphylococci and she was treated for acute bacterial endocarditis. During the course of antibiotic therapy a new Grade II/VI diastolic murmur was noted at the left sternal border. An echocardi-

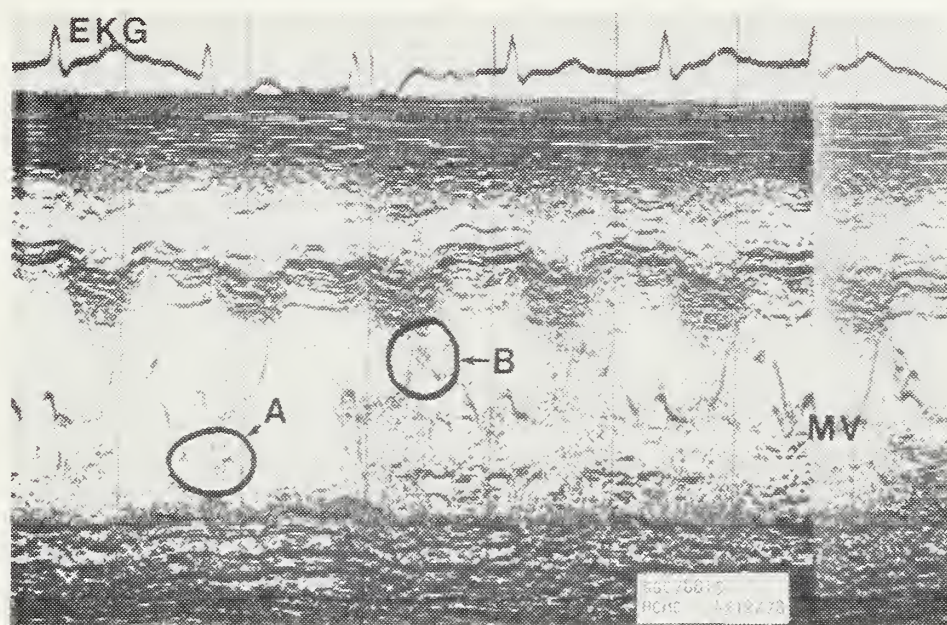


Fig. 11 — Echogram from 67 year old male with acute inferior myocardial infarction and ruptured papillary muscle. MV = Mitral Valve. Markedly abnormal mitral valve motion is noted in late diastole and systole (circle A) and early diastole (circle B) with wide excursions and irregular and inconsistent motion with each cardiac cycle.

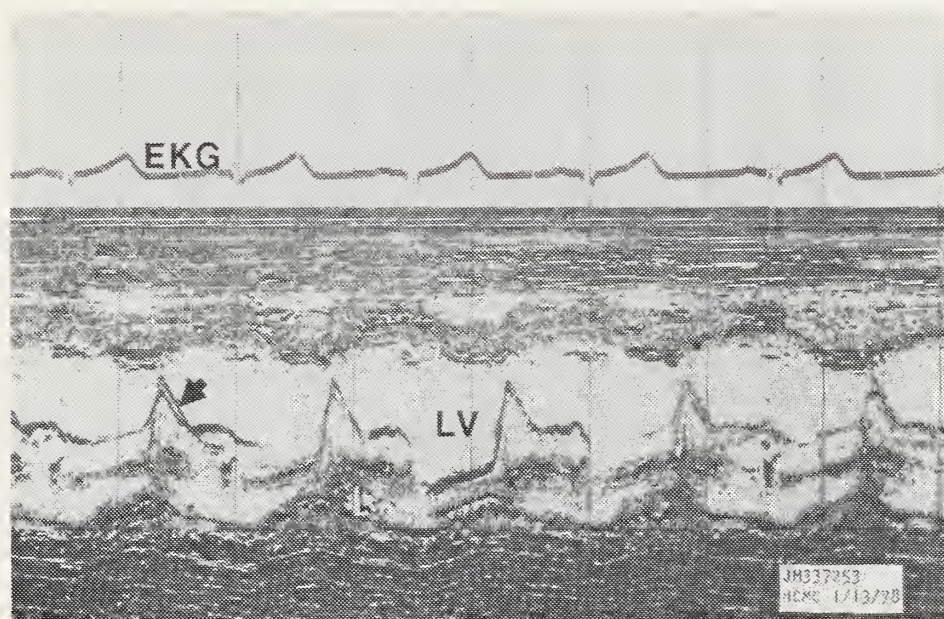


Fig. 12 — Echogram from 15 year old male with acute staphylococcal endocarditis involving the mitral valve. LV = Left Ventricular Cavity. Closed arrow indicates the anterior mitral valve leaflet in diastole. Open arrow indicates the posterior mitral valve leaflet in diastole. Dense, shaggy echoes are associated with the posterior mitral valve leaflet, indicating a vegetation.



gram obtained after she had completed a six-week course of IV antibiotics (Figure 13) demonstrated dense diastolic echoes with high frequency vertical fluttering noted in the left ventricular outflow tract and proximal aorta. Although these could represent aortic valve vegetations, their position below the aortic valve level in the left ventricular outflow tract supports the diagnosis of a ruptured or perforated aortic valve leaflet.<sup>17</sup> At the time of aortic valve replacement a torn noncoronary cusp was found without evidence of vegetative lesions.

Acute aortic insufficiency can have devastating hemodynamic consequences. We have already noted examples where echocardiography was of value in

assessing the etiology of acute aortic insufficiency. The echocardiogram shown in Figure 14 is from a 60-year-old female 12 months after aortic valve replacement. She presented with acute pulmonary edema which quickly progressed to cardiogenic shock. A new Grade III/VI diastolic murmur was present along the left sternal border. An electrocardiogram demonstrated a P-R interval of .18 sec., left ventricular hypertrophy, and nonspecific ST and T wave changes. The echocardiogram recorded at the mitral valve level demonstrates premature closure of the mitral valve (Figure 14). The mitral valve closure point precedes the onset of the QRS complex. Premature mitral valve closure in the presence of acute aortic insufficiency

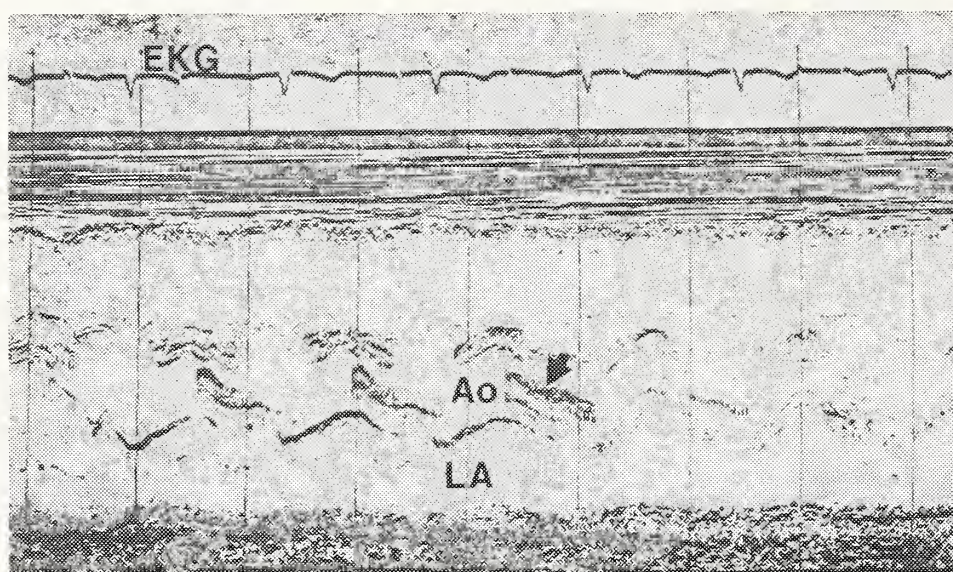


Fig. 13 — Echogram from 52 year old female with clinical evidence of aortic insufficiency after treatment for acute staphylococcal endocarditis involving the aortic valve. Ao = Aortic Root. LA = Left Atrium. Closed arrow indicates high frequency fluttering echoes in the proximal aorta. Surgical findings confirmed a flail aortic valve leaflet.

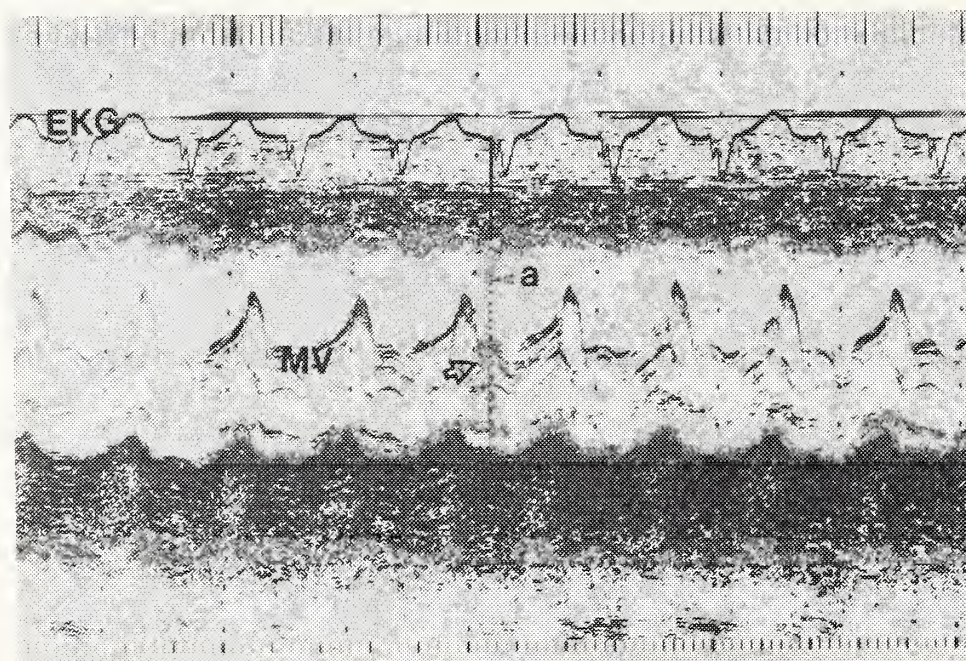


Fig. 14 — Echogram from 60 year old female with partially dehiscid prosthetic aortic valve and acute severe aortic insufficiency. MV = Mitral Valve. Line "a" indicates the timing of the onset of the QRS complex. Open arrow indicates premature closure of the mitral valve.



during sinus rhythm and a normal PR interval indicates a hemodynamically precarious situation and is very helpful in identifying patients who need acute aortic valve replacement.<sup>18,19</sup> Emergency surgery was performed with the findings of prosthetic aortic valve dehiscence of approximately 75% of the sewing ring. Hence, echocardiography is of diagnostic and prognostic value in patients presenting with acute aortic insufficiency, and should be obtained early in the course of such patients.

### Summary

In this review, we have seen that echocardiography can be of great value in the evaluation of selected patients in urgent or emergent clinical situations.

Echocardiography is helpful in leading to the correct diagnosis in clinical situations where obstruction to blood flow is suspected, as in cardiac tamponade, intracardiac tumor, or prosthetic mitral valve dysfunction. In addition, echocardiography can be of value when acute or subacute anatomical changes occur such as aortic dissection, rupture of chordae tendineae or papillary muscles, or bacterial endocarditis. In selected clinical situations, it is possible to make therapeutic decisions based on clinical and echocardiographic findings alone.

### Acknowledgments

Dr. Randall Johnson provided the clinical and echocardiographic data for the patient whose echo appears in Figure 14. Ms. Barbara Nelson provided secretarial services.

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### Cover Photograph

#### "Jack Frost Artistry"

The cover photograph "Jack Frost Artistry" was taken by Dr. Reinhold Goehl in Wirth Park, Minneapolis, at about mid-day in December, 1979, when the entire metropolitan area was enveloped in fog and all motionless exterior surfaces were covered with a delicate frost. His camera was a Nikon-FE with a 55 mm. lens. He was using Ektachrome 64, his favorite film.

Dr. Goehl has been a photography fan for years, and one of his favorite hobbies is hiking through the woods of Minnesota exploring and photographing Mother Nature's handiwork. Also, he has been a wildlife hunter for a long time but a few years ago gave up firearms and since then has spent many hours shooting at animals with his camera.

His greatest honor in photography was being awarded the grand prize in the 1980 "Diversion" magazine (for physicians at leisure) photo contest. The magazine stated that there were over 13,000 entries in the contest.

Dr. Goehl has been practicing ob-gyn in the western Minneapolis suburbs for the past twelve years.



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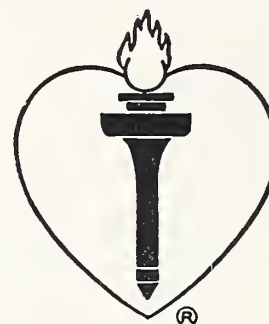
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# Echocardiography of Valvular Heart Disease

## Evaluation of Heart Murmurs

PRADUB SUKHUM, M.D.\*; JOHN W. McBRIDE, M.D.\*; LINDA A. LONG, M.D.\*; and BRIAN C. CAMPION, M.D.\*

Echocardiography provides information regarding anatomy and physiology of the heart and its structures non-invasively. Certain parts of all of the heart valves can be recorded. These properties make echocardiography a better technique to detect and evaluate the hemodynamic effect of valvular heart disease. Although at present, there have been many papers on the two dimensional echocardiographic technique which appear quite promising, this paper will review the M mode echocardiographic technique. For best results, echocardiograms should be used with other clinical and laboratory data. Utilizing proper technique and criteria to reach the diagnosis as well as awareness of echocardiographic sensitivity and specificity for various diseases or conditions are very important.

**T**HE BEST NON-INVASIVE method for detecting valvular heart disease and assessing its hemodynamic effect is undoubtedly echocardiography. Almost all cardiac valvular disease produce some kind of audible murmurs. Utilizing M mode echocardiography to help

identify the defected valves from different types of murmurs in adult patients is the purpose of this review. Table 1 and Table 2 list the types and locations of the heart murmurs for an outline. More comprehensive echocardiographic and phonocardiographic information is available from few good recent publications.<sup>1-6</sup>

Heart sounds from cardiac apex is almost always heard better with the patient on left lateral decubitus of

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Fig. 1(A) — Normal mitral valve echo showing anterior leaflet (aMV) and Posterior leaflet (pMV) motion throughout cardiac cycle as referenced by electrocardiogram. The diastolic (EF) slope and A wave are labelled. All the scales used represent 1 cm in height and half a second in duration. (B) — Mitral stenosis with some fibrotic thickening and/or calcified. The EF slope is not much decreased. The A wave amplitude is decreased but the excursion of aMV is relatively good. Notice the posterior leaflet motion. (C) — Mitral stenosis with marked thickening and/or calcification. The excursion is decreased. The A wave is not seen because of atrial fibrillation.



varying degree. The rumbling diastolic murmur from this position is usually from a chronic rheumatic mitral stenosis in adult patient. Historically this is one of the first echocardiographic cardiac diagnostic application.<sup>7</sup> The important mitral valve echo changes which usually occur together are; a. decreased early diastolic (EF) slope of the anterior leaflet, b. thickening (fibrotic and/or calcified) of the mitral valve, c. posterior leaflet motion concordant with the anterior leaflet in diastole,

TABLE 1

**A. Apical diastolic low frequency (rumbling) murmur (M)****More common****Mitral stenosis M.****Less common****Austin Flint M.****Short M. in patient with significant mitral regurgitation without mitral stenosis (Figure 2)****Rare****Left atrial myxoma with apical diastolic M.****B. Apical systolic high frequency M. (either holosystolic or late systolic M.)****Chronic rheumatic mitral regurgitation M.****Prolapsed mitral valve syndrome (include rupture chordae tendineae with mitral regurgitation M.****Mitral regurgitation M. associated with congestive cardiomyopathy****Mitral regurgitation M. due to "papillary muscle dysfunction" in case of ischemic coronary artery disease (include papillary muscle rupture complicating acute myocardial infarction)****M. associated with calcified mitral valve annulus****Mitral regurgitation M. from infective endocarditis****Mitral regurgitation M. from IHSS**

TABLE 2

**A. Ejection systolic murmur (M) at the cardiac base or left sternal border.****In younger patients****Functional or innocent M.****M in chest wall deformity patient.****Congenital bicuspid aortic valve M.****Congenital aortic stenosis M.****Supra and subvalvular aortic stenosis M.****Pulmonary valvular stenosis M., isolate or combine with other congenital lesions.****Subvalvular or supravalvular pulmonic stenosis M.****In young through old patients****IHSS****In older patients****Calcific aortic stenosis M. from various etiologies****Fibrotic thickening and/or calcification of aortic valves base with or without calcified mitral valve annulus.****B. Systolic M. along the lower left sternal border****Ventricular septal defect M.****Tricuspid regurgitation M. from various causes****C. High pitched blowing decrescendo diastolic M. at cardiac base or sternal borders****Aortic regurgitation M.****Pulmonic regurgitation M.**

d. decreased mitral valve and "A" wave excursion of the anterior leaflet<sup>8</sup> (Figures 1B, 1C). Some of these findings when found isolated may be associated with other conditions<sup>9,10</sup> (Figures 1D, 1E, 1F). It is true that many cases of mitral stenosis, the diagnosis can be made with good physical examination alone. There are also some difficult cases that echocardiogram may be very helpful, an example is illustrated in Figures 2, 1E, 3C. Assessing the severity of the mitral stenosis from the degree of decreasing early diastolic slope of the anterior leaflet has been suggested since the earlier literature with some degree of overlapping.<sup>7</sup> It is now believed to be inadequate<sup>11</sup>, and the two dimensional echocardiography appears to be more accurate when properly done.<sup>12,13</sup> Changes suggest right ventricular hypertrophy or pulmonary hypertension may indicate significant chronic hemodynamic effect of the diseased mitral valve. In addition, echocardiogram may be helpful in: determination of left atrial size, particularly in relationship to atrial fibrillation<sup>14</sup>; helpful in choosing type of cardiac surgery or prosthetic valve<sup>15</sup>; followup the course of the disease or after mitral commissurotomy; to mention a few.

Other apical rumbling diastolic murmur may be an Austin Flint murmur associated with aortic regurgitation. The echocardiogram will help differentiate from mitral stenosis by the absence of mitral stenosis pattern and the presence of mitral valve fluttering in some cases.<sup>16</sup> (Figure 3I). Left atrial myxoma is a rare condition and clinically difficult to diagnose. The most common pedunculate type when the size is big can be readily picked up by echocardiogram<sup>17</sup> (Figure 1F). Patients who have apical holosystolic murmurs as well as rumbling diastolic murmurs, particularly a shorter one, may not have a rheumatic mitral valvular disease (Figures 2, 1E, 3C).

Mitral regurgitation does not have etiologic specificity like mitral stenosis in adult patients. When an adult patient is thought or suspected to have mitral regurgitation from the presence of certain types of apical systolic murmurs, we use: (a) age; (b) other associated murmurs or heart sounds; (c) history and diagnostic procedures such as ECG, chest Xray; (d) echocardiogram; to help identify the possible etiology of the mitral regurgitation. Some lesions have specific mitral valve echocardiographic findings. Those lesions that have no specific echocardiographic patterns may require different approaches. Overall echocardiogram is still considered more helpful than other methods.

Mitral regurgitation from rheumatic mitral valvular disease is always accompanying some degree of mitral stenosis. Careful physical examination should disclose some evidence of mitral stenosis as does the



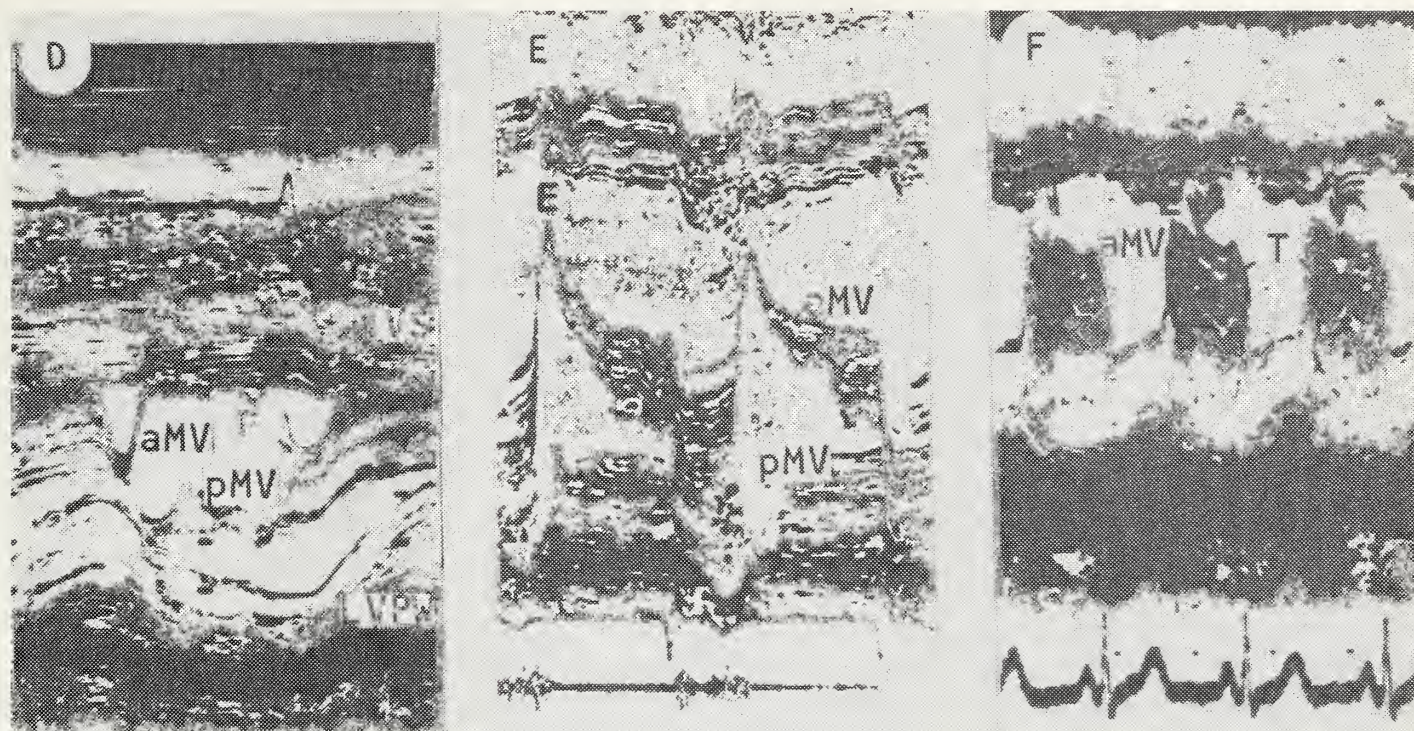


Fig. 1(D) — Decreased EF slope in a case of decreased rate of early diastolic left ventricular filling. This is a case of idiopathic hypertrophy subaortic stenosis (IHSS) with significantly decreased left ventricular compliance due to left ventricular hypertrophy. IVS = interventricular septum, LVPW = left ventricular posterior wall. (E) — Thickened mitral valve echo in a patient with prolapsed mitral valve syndrome with redundancy and possible chordal rupture. (F) — Left atrial myxoma (T) dense echo behind aMV is diastole.

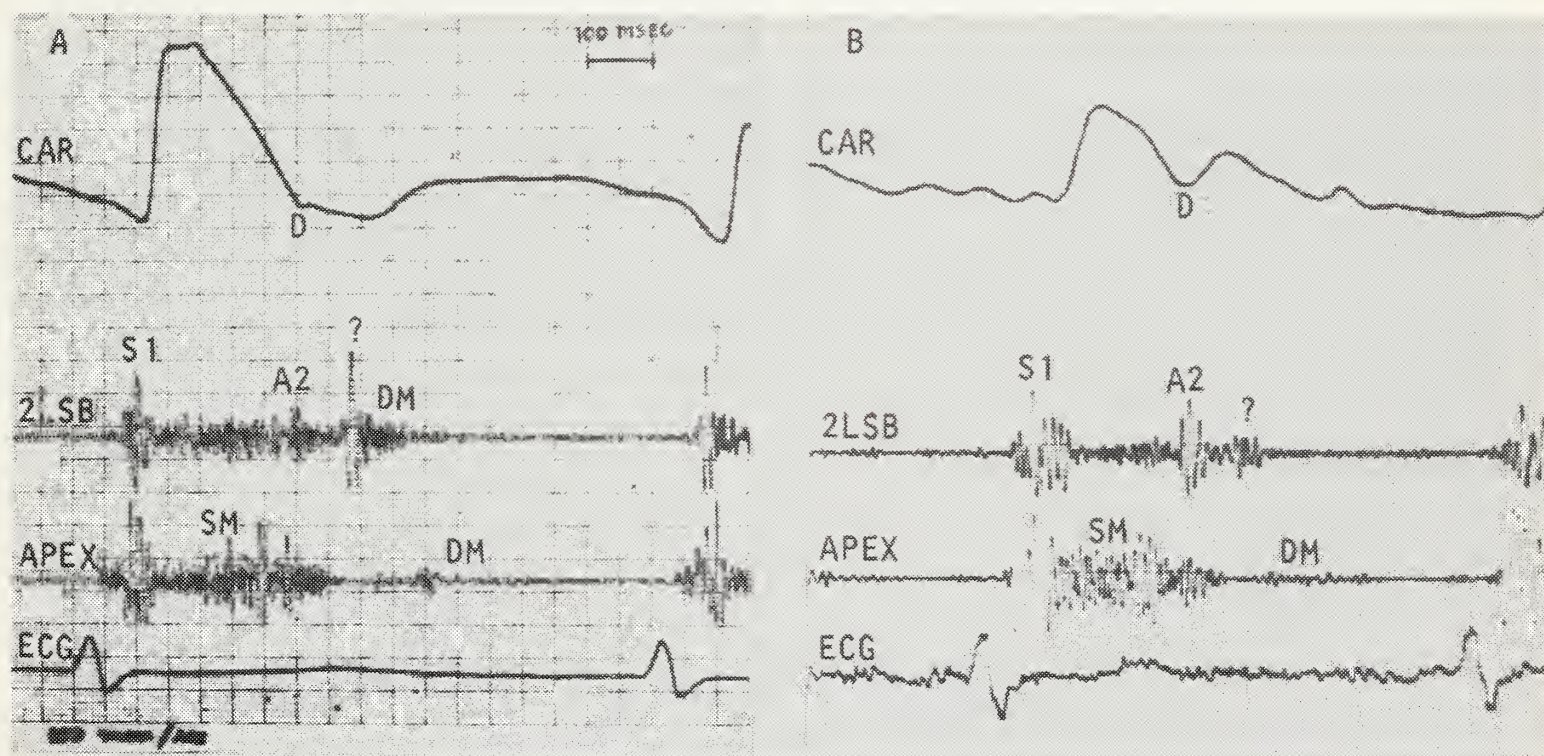


Fig. 2 — Phonocardiogram done at medium high frequency on two patients who have auscultatory findings suggesting rheumatic mitral valvular disease with mitral regurgitation and possible mitral stenosis murmur. There may be an opening snap (?) on both patients. Patient A has echocardiogram on Figure 1E. Patient B has echocardiogram on Figure 3C. Both of them show mitral prolapse syndrome. CAR = carotid pulse, D = diastolic notch, 2 LSB = second left sternal border, S1 = first heart sound, A2 = aortic closing sound, SM = systolic murmur, DM = diastolic murmur.



echocardiogram. Some cases may not have significant decreased early diastolic slope<sup>18</sup> (Figure 3A). Those who have more severe mitral regurgitation, the left ventricular study may show pattern of volume load.

The most common mitral valve defect in young

females, as many as 6%<sup>19</sup>, is the prolapsed mitral valve syndrome. Whether some of these echocardiographic findings are a normal variant is not well clarified.<sup>20</sup> Clinically when they clearly have mid or late systolic click(s) with or without apical systolic murmur, the

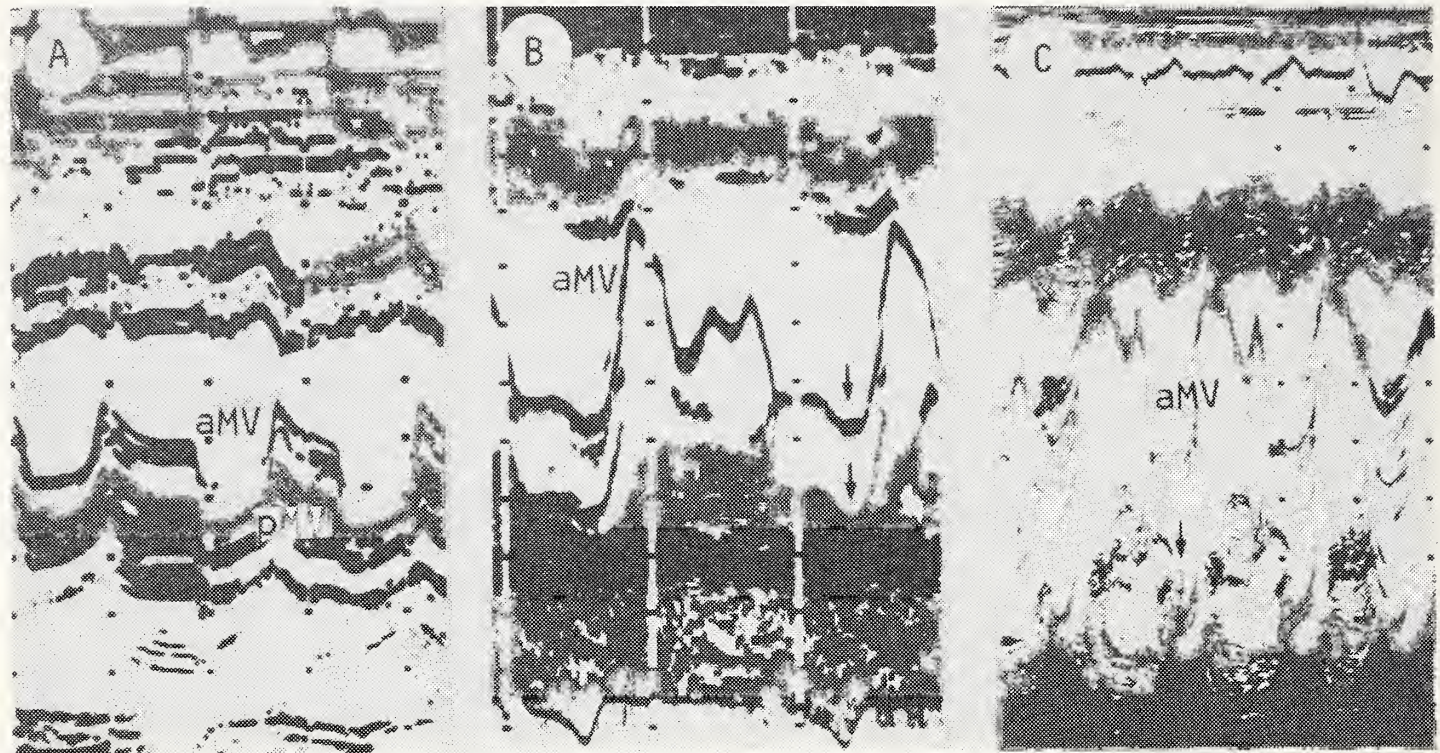


Fig. 3(A) — Rheumatic mitral valvular disease with both mitral regurgitation and mitral stenosis showing more rapid early diastolic (EF) slope. (B) — Prolapsed mitral valve syndrome showing what looks like both aMV and pMV late systolic prolapse. In most of the cases, however, it is difficult to identify separate leaflet in systole with certainty. (C) — Prolapsed mitral valve syndrome in the same patient with phonocardiogram of Figure 2B.

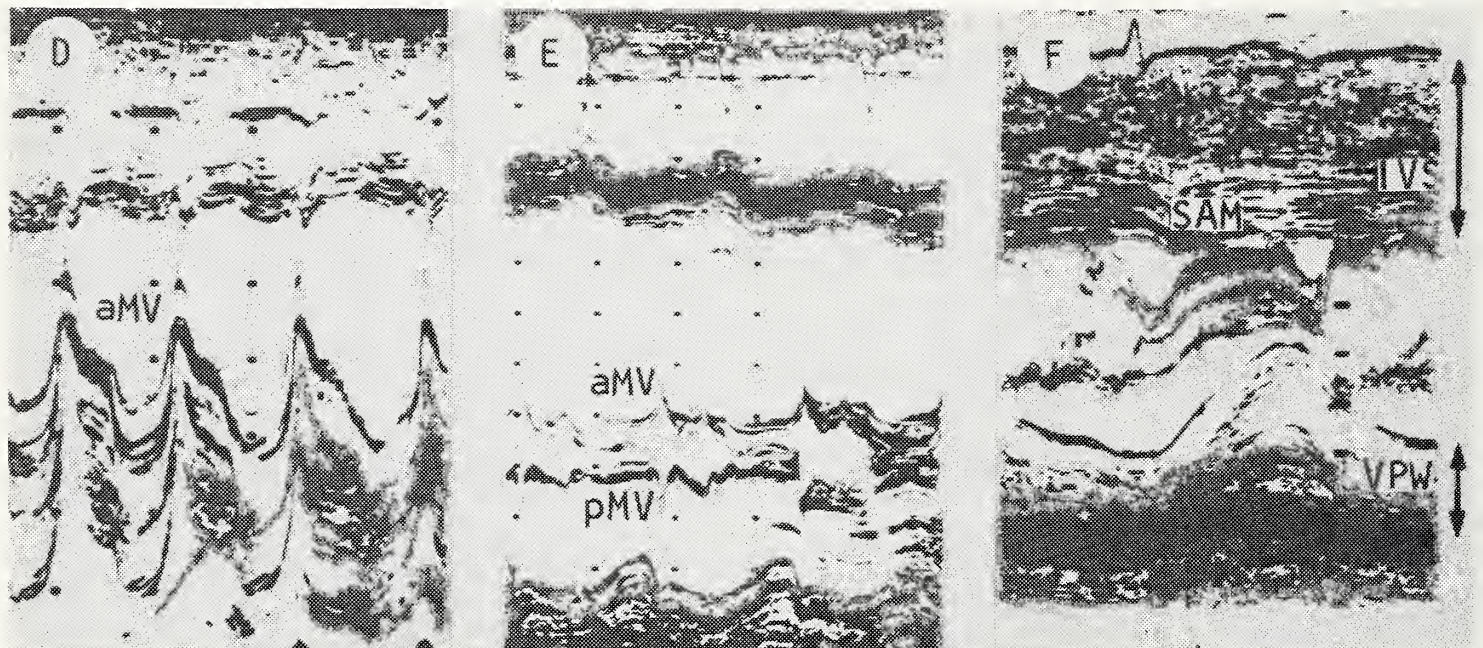


Fig. 3(D) — Prolapsed mitral valve syndrome with pMV redundancy, thickened and chordal rupture confirmed at post mortem. The pattern may look like mobile tumor in left atrium. (E) — Echocardiogram from a patient with congestive cardiomyopathy with mitral regurgitation murmur. The mitral valve is more or less "float" in left ventricular chamber. The aMV and pMV is mirror image to each other and separation is decreased. There may be multiple echo in systole. (F) — Echocardiogram from an IHSS patient (same as Figure 1D) showing asymmetric septal hypertrophy, systolic anterior motion (SAM) and aMV and small normal left ventricular internal dimension.



diagnosis is not difficult. When the only murmur is presented, except for classic late systolic murmur, the echocardiogram may help differentiate the prolapsed mitral valve from other lesions. There are variable echocardiographic spectrum for this condition<sup>21</sup> (Figures 3B, 3C, 3D). It should be emphasized that strict echocardiographic technique and criteria is required to prevent false positive diagnosis. The specificity and sensitivity may be improved with two dimensional echocardiogram<sup>24</sup>. Some cases have thickened and multiple hooding mitral valve creates a thick echo (Figure 1E). The others with posterior chordal rupture together with the above phenomenon may produce echo simulation left atrial tumor (Figure 3D). Fluttering of anterior leaflet in both diastole and systole has been reported in cases of anterior chordal rupture.

Congestive cardiomyopathy with dilated left ventricle may produce mitral regurgitation. Although the mitral valve echo may look slightly different from normal (Figure 3E). This abnormality does not necessarily explain the mechanism of mitral regurgitation which is not well understood. The diagnosis may be assumed by the presence of mitral regurgitation murmur in case of congestive cardiomyopathy as confirmed by echocardiogram. Levisman has suggested that normal or increased interventricular septal motion is associated with mitral regurgitation in

this condition.<sup>25</sup> The same approach may be applied as in case of papillary muscle dysfunction causing mitral regurgitation murmur. Because of the lack of a specific abnormal mitral valve echo in this condition, the diagnosis is suggested when there is the combination of: (a) mitral regurgitation murmur; (b) diagnosis of coronary artery disease particularly during ischemia or post myocardial infarction; (c) normal mitral valve echocardiogram. Some of these patients may have patterns of congestive cardiomyopathy with segmentally abnormal left ventricular wall motion. One fatal condition which may be in the spectrum of this condition is papillary muscle rupture associated with acute myocardial infarction. Two dimensional echocardiogram may be helpful in this situation.

Non rheumatic calcified mitral valve annulus is often associated with other degenerative changes or calcification at the base of the aortic root or aortic valve. Pathologically they are the most common findings among the elderly who have systolic murmur during life.<sup>26</sup> Because of much higher echocardiographic diagnostic sensitivity as compared to chest Xray<sup>27</sup> (Figure 3G), this condition has now been recognized more in older patients. Some of them may have loud murmur over the left precordium suggesting both apical holosystolic murmur as well as ejection murmur over left sternal border or cardiac base. In younger patients, although older one is not excluded,

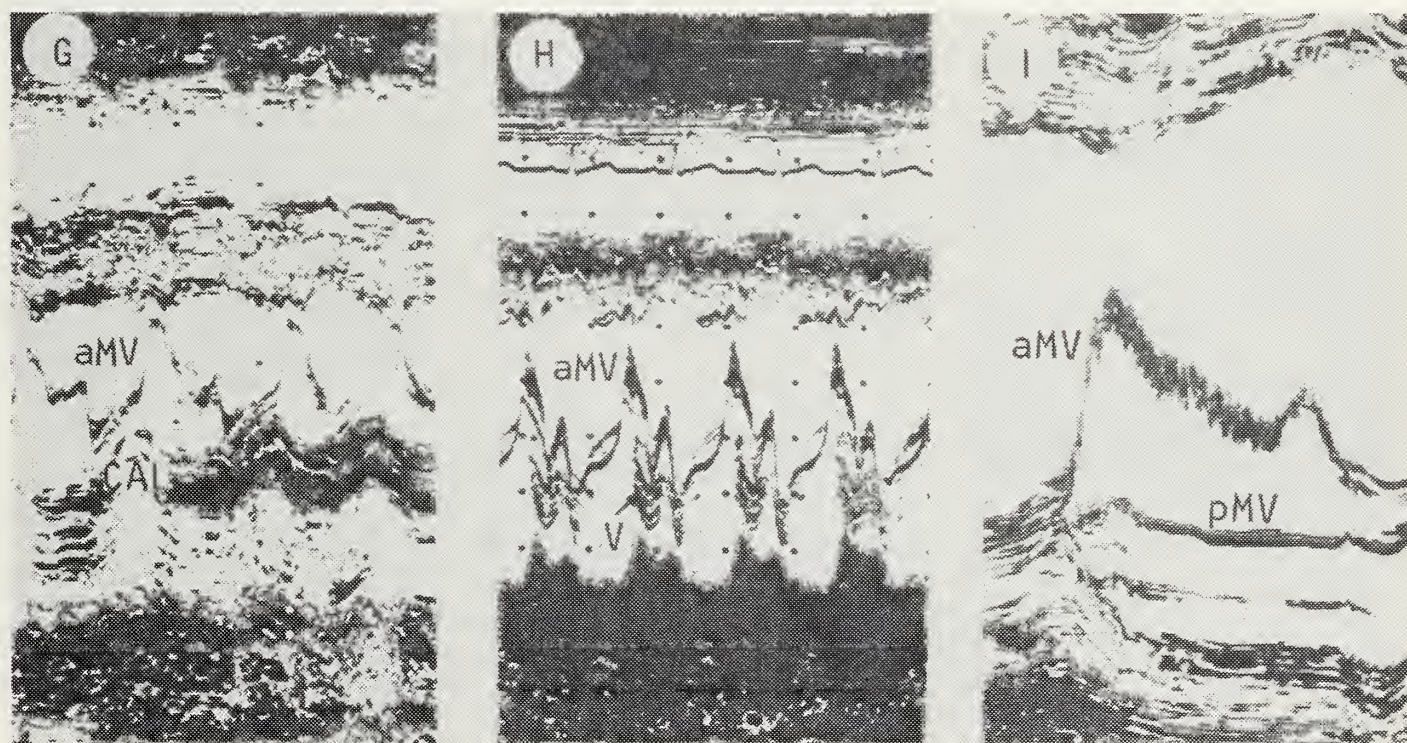


Fig. 3(G) — Calcified mitral valve annulus (CAL) of an elderly patient, showing thick and dense band of echo in between mitral valve and posterior left ventricular wall. This patient also has abnormal aortic valve echo (Figure 4C). (H) — Bacterial endocarditis in young males with prolapsed mitral valve syndrome (not shown here). The vegetation (V) is shown behind aMV. (I) — Fluttering aMV associated with aortic regurgitation. The pMV motion may be abnormal and cannot exclude mitral stenosis as well.



when the same characteristic murmur as mentioned above is present, the diagnosis of idiopathic hypertrophic subaortic stenosis may be considered. Of more importance is the characteristic change of the murmur with certain manipulations to increase or decrease left ventricular volume or contractile state. Other physical findings that may be helpful are the characteristic of the carotid pulse or cardiac apex impulse. Echocardiogram is always required to make or confirm the diagnosis for this condition (Figure 3F). Extensive review of this subject is available elsewhere.<sup>28</sup>

Bacterial or infective endocarditis effecting mitral valve may produce mitral regurgitation. The vegetation can be demonstrated by echocardiogram but the sensitivity is not good and may be too high in some reports. There are several patterns of vegetation on different valves,<sup>29</sup> and good quality echocardiogram is necessary to exclude false positive (Figure 3H). Some of those vegetations which have small size or locate in the area that might not be picked up by M mode echocardiogram may be demonstrated by two dimension technique.<sup>30</sup> Wann and associates suggested that echocardiogram may be more beneficial in prognosis.<sup>31</sup>

Ejection systolic murmur along the left sternal border or at the cardiac base in young patients may be an innocent murmur. There is no specific echocardiographic

pattern and the diagnosis is by characteristic of the murmur, location and radiation of the murmur. Then echocardiographic can exclude other obvious valvular lesions. Bare in mind that echocardiogram may miss some lesions. When the murmur is from congenital bicuspid aortic valve or congenital aortic stenosis, there is usually an associate ejection click which may require careful auscultation or good phonocardiogram. Carotid pulse characteristic and murmur radiation may be helpful. The former condition is relatively easily demonstrated by echocardiogram<sup>32</sup> (Figure 4B). While the latter is more difficult but fortunately is more rare. Other left ventricular outflow tract obstruction (exclude IHSS) such as supra valvular and subvalvular aortic stenosis are more rare conditions. However because of significant difference in surgical approach, the correct diagnosis is necessary and fortunately they can be demonstrated by M mode echocardiogram or even better by two dimensional technique.<sup>33</sup>

With increasing age, the congenital bicuspid aortic valve or rheumatic aortic valvular disease will be calcified (Figures 4C, 4D). They cannot be differentiated by echocardiogram, but presence or absence of rheumatic mitral valvular disease pattern (pattern of mitral stenosis) may suggest one etiology over another. The most common basal ejection murmur in elderly,

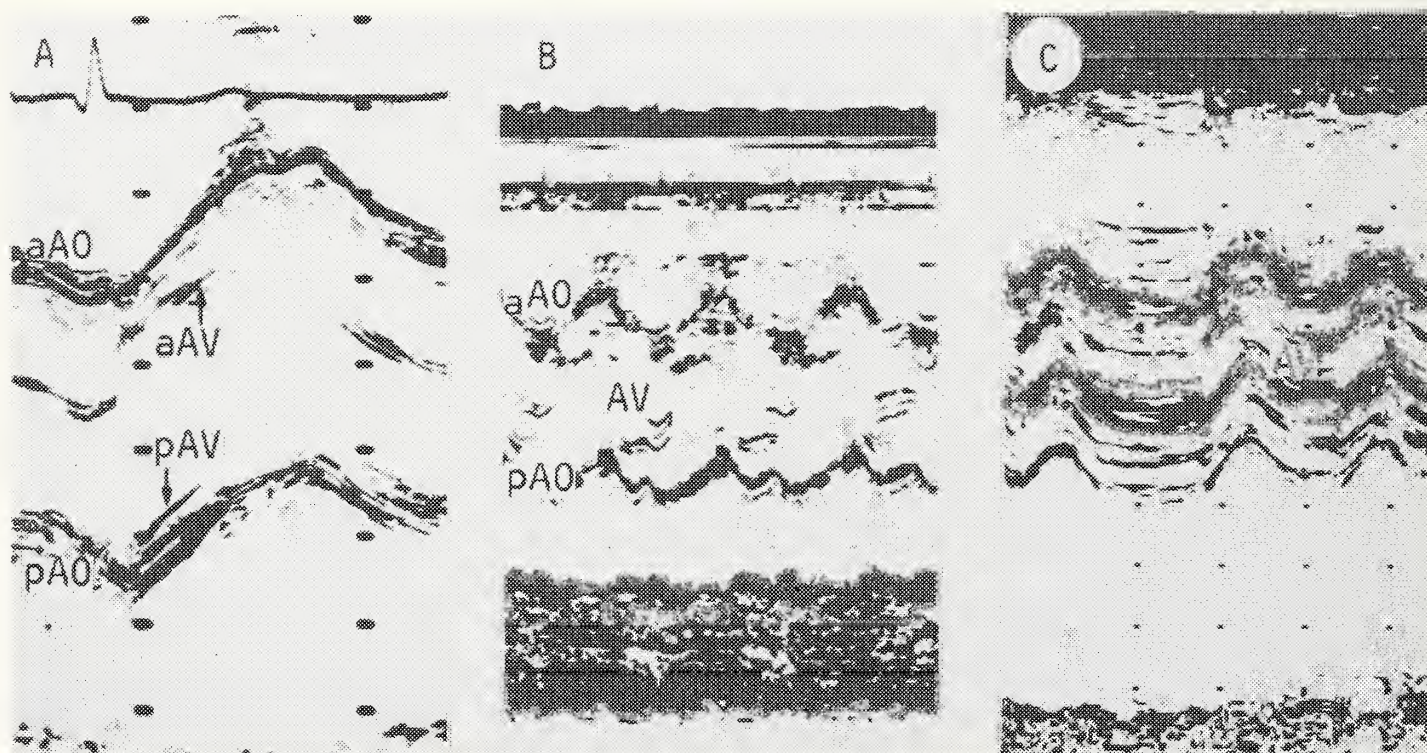


Fig. 4(A) — Normal aortic valve and aortic root pattern in a patient with aortic regurgitation (same patient as in Figure 3I). aAO=anterior wall aorta, pAO=posterior wall aorta, aAV = anterior or right coronary aortic valve cusp, pAV = posterior or noncoronary cusp. (B) — Bicuspid or unicuspid aortic valve in a teenage boy. (C) — thickened and/or calcified aortic valve (same patient with Figure 3C). Clinically this patient has no significant stenosis.



however, is probably from thickening of the base of the aortic valve cusps.<sup>34</sup> There may also be calcification and/or sclerosis of aortic valve, aortic ring or proximal aorta and mitral valve ring calcification<sup>26</sup> (Figures 3G, 4C). Assessing the severity of the aortic stenosis by aortic valve M mode echo may be difficult, but left ventricular study to assess the hemodynamic effect of the left ventricle can be helpful.

The ejection murmur from the base of the heart or the innocent murmur<sup>35</sup> thought to originate from the pulmonary valve area has recently been challenged and the left side origin was proposed.<sup>36</sup> Our experience of working up young patients for detection of "mild" isolated congenital pulmonary valve stenosis from basal systolic ejection murmur is disappointing. This is not surprising because this condition is more often associated with moderate to severe lesion which also may be suggested by other physical findings or other abnormal laboratory tests, such as systolic thrills or evidence of right ventricular hypertrophy. Both classic pulmonary valvular stenosis or infundibular stenosis associated with other congenital lesions may give some specific echocardiographic patterns.<sup>37</sup> Atrial septal defect usually has pulmonic flow murmur and wide fixed split second heart sound. When the left to right shunt is of reasonable size, the echocardiogram will demonstrate an increased right

ventricular dimension and abnormal interventricular septal wall motion. Young patients with chest wall deformity like straight back syndrome, pectus excavatum or patients with idiopathic pulmonary dilatation may have auscultatory findings as mentioned above. Chest wall examination and chest Xray may help the diagnosis.

A loud and long systolic murmur along the lower left sternal border may be found in some cases of prolapsed mitral valve in which the murmur radiates toward the medial line, possibly due to the direction of the mitral regurgitation jet stream. Small ventricular septal defect can also produce this murmur and cannot be detected by echocardiogram but the condition is rare. The presumptive diagnosis may be by exclusion of other lesions that can be echocardiographically demonstrated. Tricuspid regurgitation usually has other clinically associated conditions or findings to help the diagnosis such as the characteristic of venous pulse wave.

High pitch blowing decrescendo murmur are from either the more common aortic regurgitation or the less common pulmonic regurgitation which is usually due to pulmonary hypertension. In younger patients, with aortic regurgitation, the aortic valve echocardiogram may show the pattern of congenital bicuspid aortic

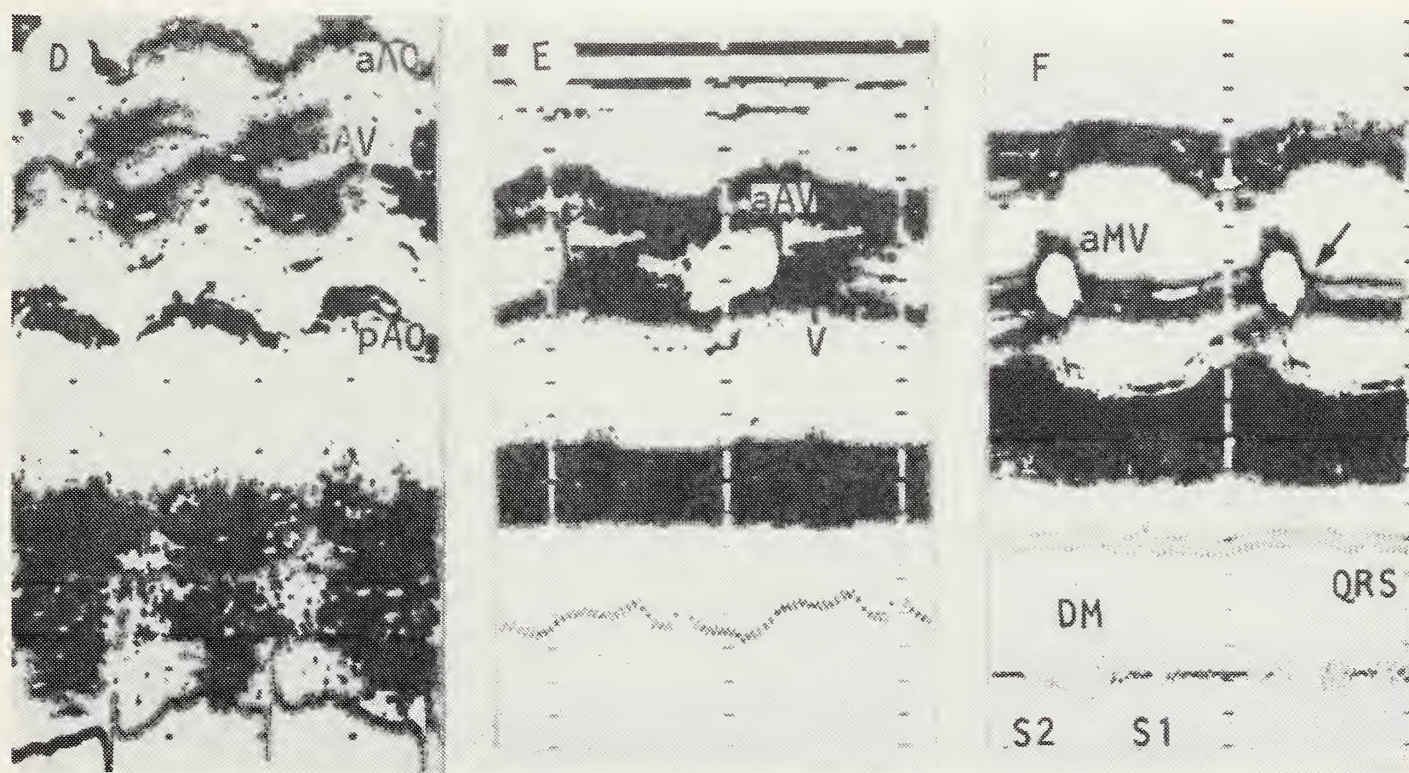


Fig. 4(D) — Calcific aortic valvular stenosis. This patient clinically has more severe stenosis. (E) — Bacterial endocarditis in a drug abuse young patient. The vegetation (V) is seen in diastole. (F) — Same patient as in Figure 4E showing premature closing of the mitral valve indicating acute severe aortic regurgitation.



valve or thickened and calcified secondary to other diseases. It is not uncommon, however, to have normal aortic valve echocardiogram (Figure 4A) and fluttering mitral valve associated with aortic regurgitation (Figure 3I). Hence there is no specific aortic valve echo pattern of aortic regurgitation and the echo-

cardiographic diagnosis is by presence typical mitral valve fluttering (or rarely interventricular vibration). Severity of the aortic regurgitation and/or degree of left ventricular compensation can be demonstrated by echocardiogram (Figures 4E, 4F) and decision of surgery can be relied on. Perhaps more often beneficial

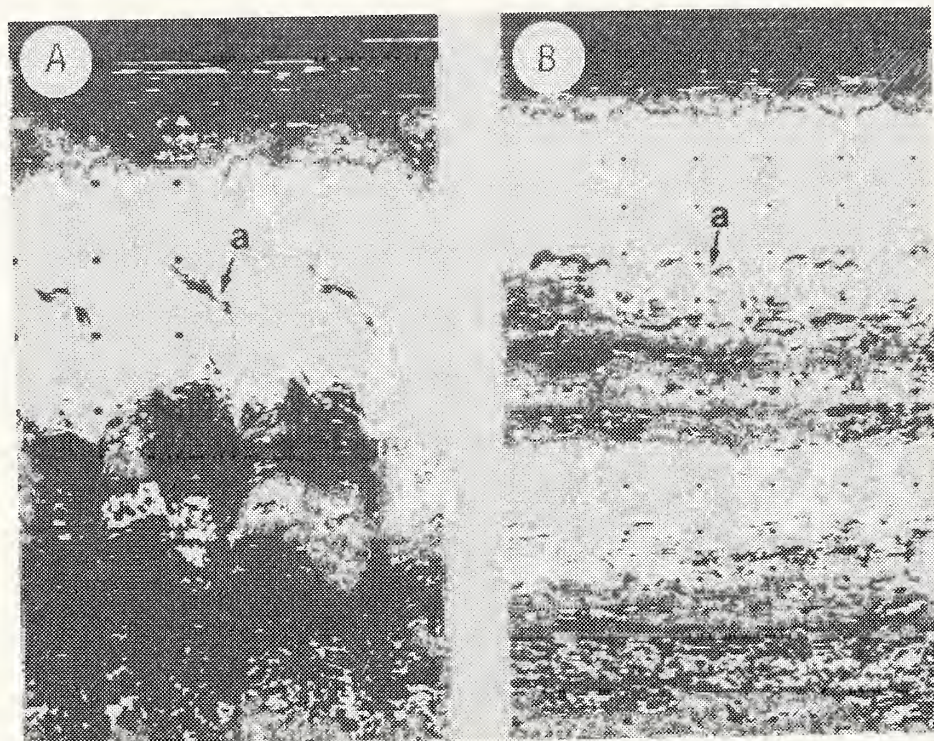


Fig. 5(A) — Normal pulmonary valve echo in a young adult with some respiratory effect. The a wave is labelled. (B) — Pulmonary valve pattern from the same patient in Figure 3(E) who has congestive cardiomyopathy with clinically documented pulmonary hypertension. The a wave amplitude in this tracing however is more than this typical case.

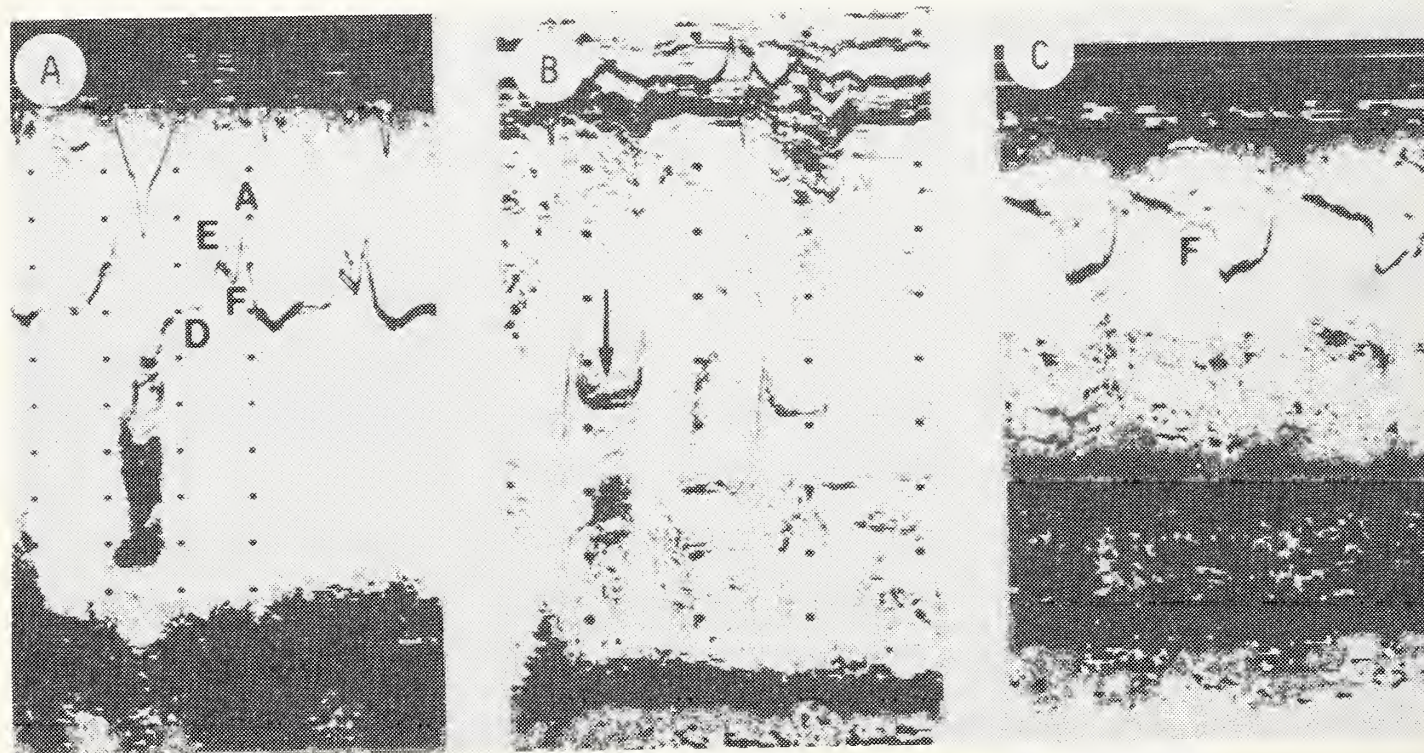


Fig. 6(A) — Tricuspid valve echo from the same patient as Figure 3E and 5B. The DE slope is abnormal and may be due to abnormal right ventricular diastolic pressure. This pattern can be due to inadequate technique. (B) — Prolapsed tricuspid valve in a patient who has mitral valve replacement from severe mitral regurgitation. (C) — Abnormal EF slope of the tricuspid valve from a patient with severe rheumatic mitral and aortic valvular disease. This may be due to abnormal right ventricular filling rate or tricuspid stenosis.



pulmonary valve echocardiographic study in adult patients is to help identify the presence of chronic pulmonary hypertension, either primary or secondary.<sup>36</sup> The latter is not uncommon in chronic left heart failure or severe mitral valvular diseases. Patients who have chronic cor pulmonale from many primary pulmonary diseases may be difficult to obtain good echocardiogram particularly the pulmonary valve. Figure 5B is the pulmonary valve echo of the same patient with congestive cardiomyopathy (Figures 3E, 6A). The pattern suggests the possibility of pulmonary hypertension, although in more typical cases the A wave amplitude is less than this. This case illustrates complete echocardiographic study which is not only helpful in diagnosis of the etiology but also hemodynamic information of both left and right heart. The tricuspid valve shows decreased DE slope and prominent "A" wave suggesting abnormal right ventricular diastolic pressure (Figure 6A). With experienced technician, both pulmonary and tricuspid valve recordings can be obtained at a reasonable or high rate. These valves, however, are usually recorded incompletely either only one leaflet or only one part of cardiac cycle (Figure 5A). When they are clearly recorded, it may suggest some dilatation of chambers involved. Primary tricuspid valvular disease is rare. Among them includes prolapsed tricuspid valve which, when present, usually associated with pro-

lapsed mitral valve as shown in Figure 6B. This patient already has mitral valve replacement for severe mitral valve prolapse. Figure 6C is the tricuspid valve echo from a patient who has severe rheumatic mitral and aortic valvular disease. This pattern may be a rheumatic tricuspid valve stenosis or the decrease EF slope may be due to abnormal right ventricular compliance. In general abnormal tricuspid valve echo can be demonstrated as those seen in mitral valve and almost all of them have been reported although at less frequency and more difficult technically.<sup>38</sup>

### Summary

This is a brief review of how to use M mode echocardiogram to help identify etiology of the common type of cardiac murmurs in adult patients. Like many other diagnostic methods, it is best to use echocardiogram along with history, good physical examination and other diagnostic procedures. When used properly, the echocardiogram not only offers many specific anatomic or pathologic diagnoses, but also physiologic or hemodynamic information much better than other non invasive procedures in the past. Recent development in this area is very rapid, mostly in two dimensional technique. M mode echocardiogram is however more difficult to perform than other non invasive methods and require experienced technician as well as experienced interpreter.

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# Pathologic Anatomy

## Virus-associated Hemophagocytic Syndrome

ROBERT J. RISDALL, M.D.\*

**This is a report of 19 patients with a reactive condition associated with active, disseminated viral infection, resulting in a clinicopathologic picture that simulated a malignant neoplastic disorder. The author suggests that cases previously reported as histiocytic medullary reticulosis may represent examples of this entity.**

THE TOPIC OF generalized histiocytic proliferations is controversial and confusing. Disorders in this category have been variously described as malignant histiocytosis,<sup>2,11</sup> histiocytic medullary reticulosis,<sup>9</sup> hemophagocytic reticulosis,<sup>4</sup> familial erythrophagocytic lymphohistiocytosis,<sup>6</sup> sinus histiocytosis with massive lymphadenopathy<sup>8</sup> and histiocytosis X (including the Letterer-Siwe and Hand-Schuller-Christian syndromes).<sup>12</sup> The clinical findings in these patients are generally similar and include fever, constitutional symptoms, lymphadenopathy and hepatosplenomegaly. Pathologically, sinus histiocytosis with massive lymphadenopathy and histiocytosis X are distinctive and can be readily separated.<sup>8,12</sup> The remaining disorders can be segregated into two groups. First are those in which the proliferating histiocytes have definite features of malignancy and little phagocytic activity. These are agreed to represent aggressive, malignant neoplasms and are best designated as malignant histiocytosis.<sup>2,11</sup> Second are those disorders where the proliferating cells have a benign, mature appearance and display marked hemophagocytosis. Cases in this latter category are often diagnosed and treated as neoplasms although their pathogenesis is unknown.

### Results

We studied 19 consecutive patients seen in the Hematopathology Laboratory of the University of Minnesota Hospitals over an 8-year-period whose bone marrow smears showed increased numbers of mature histiocytes (macrophages) with extensive hemophagocytosis. A distinct clinicopathologic syndrome emerged characterized by high fever, constitu-

tional symptoms and laboratory evidence of hepatitis and coagulopathy. Fifteen patients had pancytopenia; the other four had depression of two peripheral blood cell lines. Hepatosplenomegaly, lymphadenopathy, bilateral pulmonary interstitial infiltrates and skin rash were often present. The syndrome developed spontaneously in five pediatric patients. The other 14 patients, ranging in age from three to 61 years, were receiving azathioprine and prednisone for immunosuppression; thirteen were renal transplant recipients and one had systemic lupus erythematosus. Active infection by herpes-group viruses was documented by laboratory methods in 14 patients and by adenovirus in one. The other 4 patients were not adequately studied in this regard. Treatment consisted of supportive therapy and withdrawal of immunosuppressive drugs. Thirteen patients recovered and no recurrences have been observed. Six patients died during their acute illness.

The bone marrow smears in each case showed large numbers of mature histiocytes phagocytizing erythrocytes, platelets and nucleated cells (Figure). In 17 cases the marrow was hypocellular, indicating that



Figure — Bone marrow smear showing two mature histiocytes containing ingested erythrocytes, platelets and normoblasts. Wright-Giemsa, X 1000.

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The 1978 Ernst Award Lecture on Anatomic Pathology.

\*The annual Ernst Award for outstanding work in Anatomic Pathology by medical students, graduate students, and residents at the University of Minnesota was established in 1977 in honor of Dr. Kenneth F. Ernst through the generosity of Mr. and Mrs. Thomas R. Turner of Clearwater, Fla., and is administered by the Minnesota Medical Foundation and the Bell Institute of Pathology. Robert J. Risdall, M.D. was the 1978 awardee.



decreased production of peripheral blood elements was a major factor in the pathogenesis of the cytopenias. Lymph node biopsy in two patients and autopsy specimens in 5 patients showed a generalized histiocytic hyperplasia with hemophagocytosis throughout the reticuloendothelial system. Viral hepatitis and pneumonitis were verified at autopsy in several patients. These results have been reported in greater detail elsewhere.<sup>7</sup>

### Discussion

These 19 patients clearly suffered from a reactive condition associated with active, disseminated viral infection, as demonstrated by the clinical course observed in the majority and by the histopathologic features. However, the clinical and pathologic findings are similar to those described in previous reports as malignant neoplastic disorders.<sup>4,9,10</sup> Because they are cumbersome and have been applied to both benign and malignant diseases, we no longer use the terms histiocytic medullary reticulosis and hemophagocytic reticulosis. Careful application of standard cytologic features of malignancy is important in differentiating this reversible hemophagocytic syndrome from malignant histiocytosis. The other clinical and laboratory

features should aid in the differential diagnosis.

The pathogenesis of the hemophagocytosis is uncertain, but it appears to be a morphologic marker for disseminated or poorly controlled infection. Recently, several additional cases have been briefly reported associated with leishmaniasis,<sup>1,5</sup> typhoid fever<sup>3</sup> and brucellosis.<sup>13</sup> Therefore, it appears that the hemophagocytic syndrome may occur in association with a variety of disseminated infectious diseases. Interestingly, one of the cases associated with leishmaniasis occurred in an immunosuppressed renal transplant recipient.<sup>1</sup> Because the syndrome occurs in immunosuppressed or immunoparetic hosts in association with disseminated infections, cytotoxic chemotherapy is probably contraindicated. Rather, supportive therapy with alleviation of any identifiable predisposing factors seems to be the current treatment of choice. Since completion of this study, we have observed several additional examples of the syndrome, including a case occurring in a patient with limited Wegener's granulomatosis following radiotherapy and steroid therapy. We anticipate an increasing recognition of this syndrome, particularly in immunocompromised patients.

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# A Pathologist Views Sudden Unexpected Infant Death

RALPH A. FRANCIOSI, M.D.\*

THE UNEXPECTED DEATH of an infant raises the question, "Was the death natural or unnatural?". In 1979 there were approximately 18,000 sudden unexpected infant deaths in the United States (Table). A sudden unexpected death in an infant presents a diagnostic challenge to the pathologist. His diagnosis is dependent upon data collected from a review of the circumstances of death and a complete postmortem examination (autopsy). In approximately 50% of sudden unexpected infant deaths specific changes are observed at autopsy which establish the cause of death. However, the circumstances of death are essential, in 50%, to classify the death as either natural or unnatural; e.g. pneumonia in a neglected child. Indeed, the manner of death is essential to identify the types of unnatural death; e.g. ruptured liver secondary to accident or abuse. The autopsy should be done by a qualified pathologist and routinely include a careful external and internal examination with selective microscopic histology. Depending on the judgment of the pathologist selected cases require microbiology studies, toxicology and x-ray examination. In approximately 99% of infants dying a natural death and 95% dying unnaturally the certification of death should occur within 48 hours.

\*Director, Laboratory and Minnesota Sudden Infant Death Center, Minneapolis Children's Health Center and Hospital, Minneapolis, Minnesota.  
Presented at the 4th National SIDS Conference.

The major problems encountered in certifying a sudden unexpected infant death are: incomplete information on circumstances of death (including prior medical history), inadequate facilities for pediatric autopsies and the small number of pathologists with pediatric pathology training. I feel that these problems can be addressed by setting the following goals: strengthening death investigation systems, improved handling of pediatric autopsies, communication between the examining pathologist and family members and education of health professionals regarding the causes and consequences of sudden unexpected infant death.

When Willie Sutton was questioned as to "Why did he rob banks?", he answered, "That's where the money is!". The question of postmortem diagnoses should sit squarely in the lap of pathology. Indeed, forensic pathology can be a cornerstone for preventive health.

TABLE			
Sudden Unexpected Infant Death*			
	Natural	Unnatural	
SIDS	8500	Accident	4200
Infection	2400	Homicide	800
Malformation	1600	Suicide	0
Other	500	Iatrogenic	?
Total	13000	TOTAL:	5000

\*Infant Deaths in U.S.A. 1979.

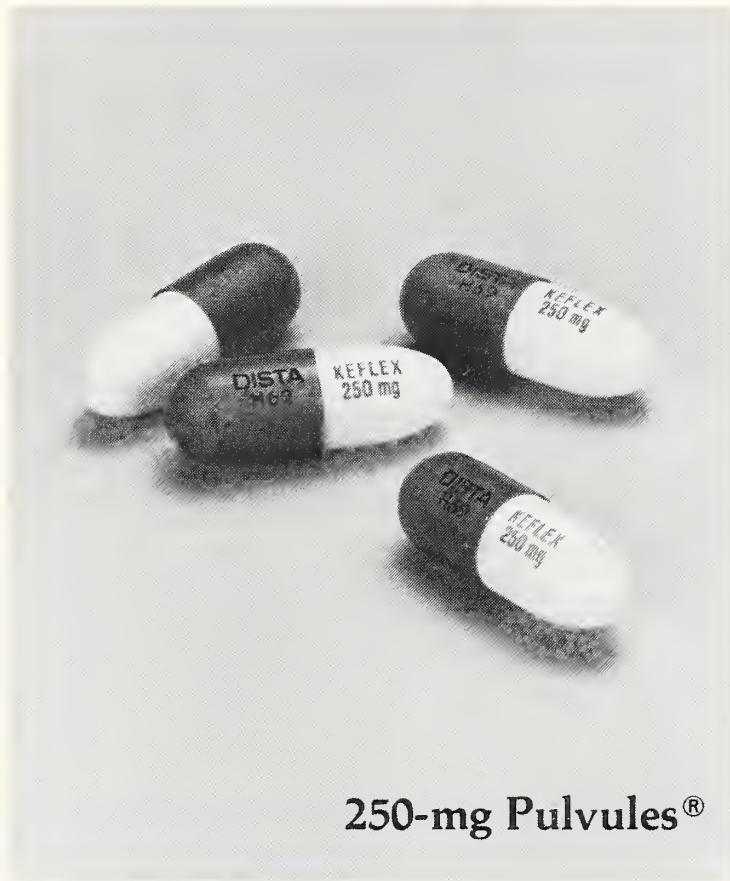
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Nominations for vacancies on the Councils of the American Medical Association that will exist on June 30, 1981, are being solicited. Physicians interested in serving or in nominating fellow physicians should submit names to the MMA Office, c/o Dr. Richard E. Barnes, 2221 University Avenue SE, Suite 400, Minneapolis, MN 55414 by January 8, 1981. If you wish further information regarding vacancies, please call the MMA office at (612) 378-1875.

Richard E. Barnes, M.D.  
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# Rheumatology Corner

## Ankylosing Spondylitis

H. S. LUTHRA, M.D.\*

**A**NKYLOSING SPONDYLITIS is a chronic inflammatory disease of unknown etiology which primarily involves the axial skeleton but can affect also the peripheral joints and other organ systems. The incidence of ankylosing spondylitis in the general population was felt to be 0.5-1:1000, but recently a survey of HLA-B27 positive 'asymptomatic' blood bank donors revealed that it may be as high as 10:1000.

Classically the clinical presentation of a patient with this disease is that of a young male 15-35 years in age with intermittent back pain. Initially the symptoms usually localize in the lumbosacral region but the whole spine may be affected. Stiffness of the paravertebral regions which appears after periods of rest and improves with physical activity can be a prominent feature. The duration of 'morning stiffness' can be a good measure of disease activity. Nocturnal back spasms, fever (generally low grade), and weight loss may be other associated symptoms. Peripheral arthritis, may, also be the presenting feature.

On examination there is loss of lumbar lordosis initially as a result of muscular spasm, but later fusion can occur in that position. There is tenderness along the paravertebral muscles, sacroiliac joints, or the spine. Usually the first motion that is lost is lumbar extension followed by lateral bending and rotation and later forward flexion. This may progress to a stooped posture from thoracic kyphosis, resulting in loss of height and chest expansion. In well advanced cases restriction of movement of the neck may be observed even during the interview.

Laboratory tests may reveal a mild to moderate normocytic normochromic anemia of chronic disease. An elevated erythrocyte sedimentation rate may be observed but is a less reliable indicator of disease activity. Over 90% of the patients are HLA-B27 antigen positive compared to 8% of the normal Caucasian population. Xray changes vary with the stage of the disease. Initially they usually are negative. The first change detected is in the sacroiliac joints but because of the age of onset of this disease (usually in the late teens and early twenties when the sacroiliac joints normally give a picture of blurred margins) this may be unreliable. Later erosions, increased sclerosis

and fusion of the joints is seen progressively. Changes in the apophyseal and costovertebral joints follow a similar pattern. Involvement of the spinal ligaments leads to 'squaring' of the vertebrae and calcification along the intervertebral and longitudinal ligaments. Other than changes in the posture and the resulting limitation of motion, involvement of the spine in ankylosing spondylitis can lead to C<sub>1</sub>-C<sub>2</sub> subluxation which is detectable on flexion-extension views of the cervical spine. A fused spine is more susceptible to trauma resulting in fractures which may be difficult to detect and can lead to pseudoarthrosis. Vertebral granulomas occur infrequently but may result in painful instability.

Involvement of the shoulders or hips in patients with ankylosing spondylitis is not uncommon leading to loss of motion and joint damage. Peripheral joint involvement may mimic rheumatoid arthritis. Ankylosing spondylitis patients can develop anterior uveitis which may occur before, during or at time of remission of the disease, and should not be overlooked as this could lead to visual impairment. Rarely some patients develop fibrobullous disease at the lung apex, aortic insufficiency, cardiac conduction abnormalities, amyloidosis, and the cauda equina lesion.

Diagnosis is made from the patient's history, physical examination and the laboratory changes and is easy in a well-established case but in a young adult it may be difficult. One may need to treat the patient as having ankylosing spondylitis if there are suggestive features even if the diagnosis cannot be established with certainty. There is no certain therapy which would halt the progress of this disease or lead to regression of the changes. The aim in management should be to make the patient comfortable, to achieve and maintain as much mobility as possible and stress posture principles aimed at avoiding fusion in a kyphotic position. Extra rest in bed in a supine position without a pillow under the head and on a very firm mattress is very important and more so during the active phases of the disease. Complete immobilization for prolonged periods, however, should be avoided since this would encourage early fusion and lead to loss of motion. Patients should be advised to hold themselves erect whether sitting or standing, sit in a straight back chair

\*Assistant Professor of Medicine, Mayo Medical School, Rochester, Minnesota.



and to avoid bending, twisting, heavy lifting and long hours of standing as much as possible. Lying prone when watching television or reading should be encouraged as this would tend to decrease development of spinal kyphosis and hip flexion contractures. Heat from a lamp or torso baker or hot showers are helpful. Exercises aimed at maintaining range of motion of the spine and peripheral joints, and avoiding flexion contractures, should be performed regularly. Accurate measurement of the height and chest expansion can be useful parameters to follow progress of the patient.

Drug therapy, mainly in the form of anti-inflammatory agents e.g. aspirin, indomethacin and other nonsteroidal anti-inflammatory agents such as naprosyn, nalfon, motrin, tolectin and clinoril can be used. Phenylbutazone used for short periods is helpful.

Corticosteroids are rarely necessary except when treating co-existing anterior uveitis or occasionally as intra-articular injections for management of a persistent and otherwise unresponsive inflammatory arthritis in a peripheral joint. As in other arthritides some patients may require joint arthroplasties if excessive damage occurs. Total hip replacement, when necessary, can be helpful to increase the patient's mobility and posture. Vertebral osteotomy may be considered as a palliative procedure for severe kyphosis.

The prognosis is generally good in patients with this disease. They should avoid jobs involving manual labor and avoid contact sports. Otherwise these patients with proper education, medical supervision and self-discipline can lead useful and productive lives.

#### References

1. Polley HF: The diagnosis and treatment of rheumatoid spondylitis. *Med Clin North Am* 39:509, 1955.
2. Luthra HS: Extra-articular manifestations of ankylosing spondylitis. *Mayo Clinic Proceedings* 52:655, 1977.

#### Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
3. Has made outstanding contributions to the Medical School, the University, the Alumni, and the community.
4. Has had a relatively long experience in the field of medical science or a related field.

Nominations for the March, 1981 awards should be sent immediately to:

Konald A. Prem, M.D., Chairman,  
Harold A. Diehl Award Committee  
Box 395, University of Minnesota Hospitals  
Minneapolis, Minnesota 55455  
(612) 373-7635

Detailed supporting documents are necessary to consider nominees, but these can be forwarded later.



# Minnesota Medical Association

## “Come To Your Senses — Quit Smoking”

D-Day 1981

RICHARD C. WOELLNER, M.D.\*

The title above is the slogan for this year's D-Day campaign. The phrase not only encourages exercising one's intellect in realizing the hazards of smoking, but suggests the problems with taste and smell that smokers develop. D-Day itself, a day when smokers are encouraged to promise to quit the habit, is a Minnesota product. It was originated in 1974 by Lynn Smith, a newspaper editor from Monticello. The day has been adopted nationally, and for Minnesota will take place on January 22, 1981.

Our collective responsibility for preventive medicine extends beyond encouraging our own patients to stop smoking — or not to start smoking. Recent studies<sup>1</sup> have shown that lung problems can develop not only in smokers, but in those unfortunate nonsmokers who are exposed to the second-hand smoke of nearby puffers. We can support our enlightened laws regarding nonsmoking areas in public buildings, and we can support public nonsmoking campaigns. This is the purpose of D-Day.

As physicians, what can we do ourselves to aid this campaign and to decrease the public health and environmental problems associated with smoking?

(1) We can make D-Day publicity available in our own offices. Posters and pledge cards are available for our use by writing D-Day Headquarters at 2750 Park Avenue, Minneapolis, MN 55407, or by calling 612-871-2111.

(2) We can refer our motivated patients to nonsmoking programs. A recent guide for these programs available in Minnesota can be obtained from the Minnesota Lung Association at 614 Portland Avenue, St. Paul, MN 55102. This booklet lists group programs available by location in the state.

(3) Some patients prefer to try to stop smoking on their own. The Minnesota Lung Association has a booklet entitled “Freedom From Smoking in 20 Days” which outlines a personal program for smoking cessation. This, and a follow-up program booklet entitled “A Lifetime of Freedom From Smoking”, will be available from the Minnesota Lung Association in January, 1981. And the American Cancer Society, Minnesota Division, has a self-help “I Quit Kit” available to individuals, without charge. Order from the American Cancer Society, 2750 Park Avenue, Minneapolis, Minnesota 55407.

All these things can help your patients “come to their senses”. Join the 1981 D-Day campaign — write D-Day, 2750 Park Avenue, Minneapolis, Minnesota 55407 for posters, pledge cards, and more information.

---

\*Chairman, Professional Education Committee and 1981 MMA D-Day Campaign.

### References

1. White, JR and Froeb, HF: Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke. *New Engl Med* 302:13, 1980.



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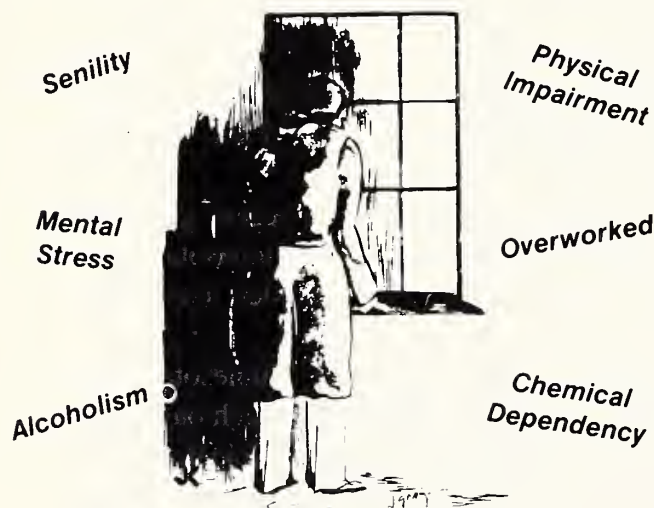
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# Minnesota Medical Association

## MMA Annual Meeting “Common Medical Experiences”

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- Antimicrobial Therapy
- Casting and Splinting Techniques\*
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- Occupational Medicine
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- Pediatric Problems
- Gastrointestinal Surgery
- Sports Medicine
- Basic Cardiac Life Support\*
- Preventive Medicine
- Sudden Infant Death Syndrome
- Life-Support Procedures\*
- Clinical Toxicology
- Pediatric Surgery
- High-Risk Obstetrics
- Rheumatology Update
- Medical Problems of SE Asian Immigrants

\*Hands-on skills workshop

NON-MEMBER SPONSORSHIP: Physicians who are not members of the Minnesota Medical Association may attend the Scientific Assembly without paying the registration fee if sponsored by an MMA member. Both members and non-members interested in the sponsorship program should contact Mr. David Luth, Director of Membership, Minnesota Medical Association, Suite 400, 2221 University Avenue SE, Minneapolis, MN 55414, 612/378-1875.

FOR FURTHER INFORMATION REGARDING THE ANNUAL MEETING, CONTACT:

Department of CME & Program Services  
Minnesota Medical Association  
Suite 400, 2221 University Avenue SE  
Minneapolis, Minnesota 55414  
612/378-1875

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### Dr. Robert H. Bösl, New MMA Board of Trustees Member

Dr. Robert H. Bösl, M.D., was recently elected to serve on the MMA Board of Trustees, representing residents and medical students. He will serve as the chairman of the Ad Hoc Committee on Residents and Medical Students.

Dr. Bösl has been active in organized medicine, both as a medical student and resident. He is a member of the AAFP and the MAFP, presently serving on the MAFP Board of Directors and has served on several committees at the HCMS, MMA and AMA.

Dr. Bösl is a resident in the Family Practice Program at Methodist Hospital, St. Louis Park. He completed medical school at the University of Minnesota where he was Vice President of the Medical Student Council. He is married and has four children.



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# Minnesota Medical Association

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James H. Sova, Assistant Executive Vice President  
Lynn R. Gruber, Director, Department of Medical Services and Research  
George C. Lohmer, Jr., Director, Department of Health Planning  
Charles W. Wiger, Director, Department of Legislative Affairs

### Department of Health Planning

#### *MMA Board of Trustees Position Statement on Federal-mandated Process of Appropriateness Review*

The concept of Appropriateness Review (AR) was contained in P.L. 93-641 (the original 1974 Health Planning Law) and P.L. 96-79 (the revised Health Planning Law). A finding of "appropriateness" is a public statement made by an HSA which means that the need of a population for an *existing* service in relation to a set of criteria, is satisfactory. A finding of "inappropriateness" results when *existing* services do not meet at least one criterion. Remedial action statements by the HSA are required if a finding of "inappropriateness" is made. Services to be reviewed include those offered by public or private hospitals, rehabilitation facilities, nursing homes, home health services, and HMOs.

There are two levels at which reviews and recommendations in the AR process can be made. They are area-wide reviews and area-wide recommendations; institutional-specific reviews and institutional-specific recommendations. There is no definition in the federal regulations as to what constitutes the difference between "area-wide" and "institutional-specific" reviews. The federal government only requires area-wide Appropriateness Review.

Statements of "appropriateness" or "inappropriateness" carry no *formal* sanctions. However, the federal regulations encourage states to pass legislation which would result in sanctions for negative review findings. Even without formal sanctions, third-party payors, lending institutions, or other agencies (e.g. rate review) may use Appropriateness Review as a basis for their own deliberations.

#### MMA Position Statement Regarding Appropriateness Review

1. The Medical Association expresses strong concern that Appropriateness Review will not prove to be a cost-effective approach to containing health care costs or assuring quality, accessible care. The net effect of Appropriateness Review, as well as other health care planning tools, can be to "franchise" certain hospitals or providers to deliver certain services, while reducing patient choice and accessibility of services. This approach to health planning has no built-in incentives for delivering cost-effective, quality care, and invites ever increasing regulatory intervention to ensure cost accountability. Competitive alternatives can be a much more effective mechanism for eliminating unnecessary duplication in the system while ensuring necessary flexibility to address changing needs.

2. Appropriateness Review as now constituted weakens locally-controlled health planning. The Medical Association reiterates its position of support for responsible local health planning. Appropriateness Review, however explicitly dictates HSA and state roles, and provides minimal opportunity for responsible local self-determination. Significant changes in federal law and accompanying regulations should be promulgated to facilitate self-determination and grant precedence to local initiatives over federally-mandated planning functions.

Many HSAs have developed a local hospital long range planning process which addresses



## DIVISION OF SOCIO-ECONOMIC AFFAIRS

many of the services envisioned to be studied in Appropriateness Review. These local planning processes will now have less flexibility in timing and outcome because of Appropriateness Review.

3. Appropriateness Review should be incorporated into the HSA planning process. The function of health planning is to provide a framework in which incentives are developed to assure the appropriate amount of cost-effective quality accessible care. Singling-out this aspect of the planning process places undo emphasis on one phase of an HSA's activity. However, since Appropriateness Review is an identifiable function mandated by the federal government, it should be well-integrated into the planning process. This means that the process to develop AR findings and recommendations remains flexible, the guidelines and criteria provide guidance, and there are frequent re-evaluations (i.e. at least annually) of the guidelines, criteria, and recommendations.

4. Appropriateness Review should be area-wide in both its findings and recommendations. Institutional-specific reviews and institutional-specific recommendations are an HSA Board option. This option should only be used when all other alternatives at trying to effect needed change have not worked and the following criteria found in the Conference Report on P.L. 96-79 can be appropriately met. Criteria suggested to be used include: (1) the nature and seriousness of the problem which makes the service inappropriate; (2) its susceptibility to change; (3) the amount of information the Agency has about the problem; and (4) judgment about how best to achieve needed change within the Agency's area. These criteria could be used by an HSA Board to determine, at the beginning of each AR cycle, for each service, whether their recommendations or findings should be area-wide or institutional-specific.

5. Appropriateness Review findings should not constitute a finding for Certificate of Need. The Health Systems Plan, as the basic and primary planning tool, should be the source document for all HSA planning and regulatory activities. Appropriateness Reviews are based on the Health Systems Plan and additional mandated criteria. Certificates of Need are also based on the Health Systems Plan, but include a different set of mandated criteria. Because of the inconsistencies in these sets of criteria, it would be inadvisable to use Appropriateness Review findings as the basis of Certificate of Need decisions.

An additional reason that Appropriateness Review should not constitute a finding for CON is based on a commitment to the planning process. Since the Health Systems Plan is the basic document for HSA planning, all recommended changes to the system should be first reflected in the Health Systems Plan.

6. Evaluation should be an integral part of Appropriateness Review. The federally-mandated five year review cycles for each service are not frequent enough to reflect changes in the delivery system. Thus, Appropriateness Review findings and recommendations should indicate that present services meet current guidelines and criteria. Ongoing HSA review will re-assess guidelines, criteria, and recommendations on a periodic basis.

The MMA supports actions by Health Systems Agencies which would improve local health planning. As now promulgated, Appropriateness Review specifically dictates the Health Systems Agency's and the state's role, and provides minimal opportunity for responsible local self-determination. Appropriateness Review is just one example of a trend, gaining momentum, which makes the local HSAs an extension of the federal health planning effort, rather than a local advocate of responsible local planning.

### Department of Medical Services and Research

Pursuant to legislation enacted during the 1980 Legislative Session, the Minnesota Department of Public Welfare (DPW) is in the process of developing a new version of "Rule 64." The rule will set standards for the Surveillance and Utilization Review (SUR) program. The SUR Division is responsible for identifying and investigating incidents of



## DIVISION OF SOCIO-ECONOMIC AFFAIRS

suspected fraud, theft, and abuse which may occur in the Medical Assistance, General Assistance Medical Care, and Catastrophic Health Expense Protection Programs.

On November 3, 1980 interested groups and individuals were given an opportunity to discuss a first draft of the newly revised Rule 64. MMA staff attended the meeting. After hearing comments and criticism concerning certain provisions of the first draft of Rule 64, staff at DPW agreed to take the information under advisement and to revise the Rule accordingly.

The Department of Public Welfare abandoned its efforts to establish a 1978 version of Rule 64 due to insufficient statutory authority to promulgate the rule proposed in late 1978. A bill passed in 1980 which alleviates that problem.

The Department of Medical Services & Research will provide testimony at the formal public hearing which is scheduled for January 14, 1981.

### Department of Legislative Affairs

On January 6, 1981, the Minnesota legislature will convene. As noted in the following account, nearly all of the issues the MMA anticipates addressing have appeared in previous sessions, though it is expected that there will be some surprises.

Overall, the MMA will be sponsoring this legislation:

- (1) Drug product identification (described in October, 1980 MINNESOTA MEDICINE).\*
- (2) Model determination of death act.
- (3) Pre-school screening act revisions.
- (4) Mandatory use of motorcycle helmets.
- (5) Mandatory use of child passenger restraints.

Additionally, the MMA may sponsor measures pertaining to the Certificate of Need Act, the data privacy law and comprehensive K-12 health education programs.

Key proposals that the MMA will vigorously oppose include

- (1) Expanding the scope of chiropractic practice. The "blood withdrawal" lawsuit could result in an adverse opinion for chiropractors, and thus, a legislative remedy is probably in the offing.
- (2) Allowing optometrists to use drugs for diagnostic purposes.
- (3) Mandating HMOs to provide chiropractic and optometric services.
- (4) Allowing direct third party reimbursement to nurse practitioners for performing certain procedures.
- (5) Requiring state regulation of all Xray machine operators.
- (6) Allowing direct action lawsuits. This proposal would permit plaintiff's attorney to name the defendant's insurance company as a direct party in professional liability actions.
- (7) Redefining when the statute of limitations begins to toll for professional liability actions against physicians.

The Department of Legislative Affairs is working on these issues, and you are encouraged to call if there is any information you need in communicating with your area legislators.

### *Physician and spouse involvement is key to MMA Legislative Program.*

The Department of Legislative Affairs emphatically encourages you to get involved since lack of action on your part dilutes our effectiveness and leads to the passage of proposals like those mentioned above which MMA is opposing. For example, if chiropractors across the state participate in campaigns and continually express their concerns — and you don't say a word to your local legislators — how do you think a legislator is going to vote when faced with this issue.

\*Page 6.



## DIVISION OF SOCIO-ECONOMIC AFFAIRS

If you want to help, please note the following:

- (1) **KNOW YOUR LOCAL LEGISLATORS.** Surprisingly, many physicians don't know who their state representative and state senator are. To find out, just call your city hall, or call your Department of Legislative Affairs.
- (2) **MEET WITH YOUR LOCAL LEGISLATORS.** It is imperative that you develop a rapport with them. In many cases, your legislator may already be familiar with you because of your work and community standing. Encourage your local medical society to set up meetings with area legislators.
- (3) **READ THE PHYSICIANS LEGISLATIVE BULLETIN AND OCCASIONAL LEGISLATIVE ALERTS.** The thrust of our legislative communication is provided in these publications. If you haven't received these materials and are now interested, please call the Department of Legislative Affairs and you'll be put on the mailing list.
- (4) **SUPPORT MINNPAC.** The Minnesota Medical Political Action Committee (MINNPAC) reviews legislative candidates and supports those candidates who are open-minded toward medicine. Just as organized labor, chiropractic and other groups have their "PAC" to represent their interests, you have MINNPAC. Support it.

Your interest in legislative matters is greatly appreciated. While such involvement does take some time, many physicians and auxiliaries properly recognize that such time spent is necessary and worthwhile.

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### **The Butcher, the Baker, the Candlestick Maker**

The MMA Aux. has recently purchased . . . The Butcher, the Baker, the Candlestick Maker, a 27-minute, 16 mm sound/color motion picture that presents alcoholism as a treatable disease. Its target is educating the public and physicians about the nature of the problem and the urgency of early detection and treatment.

The film includes a cine-play called "I'll Drink to That!" which dramatically illustrates the effect of alcoholism on a couple and the child born to them. The play's dual ending demonstrates the importance of early diagnosis by a physician. It was created by Dr. Joe Norquist, John Goodell and Tom Kohout, produced by Pro-7 Productions, Inc. and sponsored by St. John's Hospital, St. Paul, Minnesota.

The film is available on a loan basis by contacting: Karen Tourdot, Minn. Med. Assn. Aux., 2221 University Ave. S.E., Suite 400, Minneapolis 55414.

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### **Have you read NEWSPAGE lately?**

If you haven't been reading NEWSPAGE you are missing a good source of information. The monthly newsletter from Harold Brunn, MMA Executive Vice President, contains up-to-date reports on MMA programs, legislation, public health concerns, education programs, member services, and publications.

Remember to look for NEWSPAGE in your mail the first week of each month. NEWSPAGE will keep you better informed.





# MINNPAC

Medicine's Voice in Government

## MINNPAC Membership Reaches Record High, Election Yields Surprising Results

Recognizing the value of political involvement, physicians joined MINNPAC in record numbers in 1980. More than 1140 physicians and auxiliaries enrolled prior to the November elections. This figure represents about 28% of the MMA membership. These contributions ranked MINNPAC third behind the Minnesota AFL-CIO and the Minnesota Education Association in candidate support.

The record membership allowed the MINNPAC Board to: (1) Contribute \$83,855 to legislative campaigns. (AMPAC contributed \$36,000 to congressional races.) (2) Support 101 of the 134 successful House candidates (75%) and 43 of the 67 winning Senate candidates (64%). (3) Distribute the "Physician-Auxiliary Election Preview" to members. The "Preview" highlighted candidates supported by MINNPAC.

With both the Senate and House standing for election again in 1982 after the districts are reapportioned, MINNPAC Board members will begin aggressive membership solicitation early in 1981. Included in the membership drive will be: (1) Increased emphasis on clinic payroll deduction plans for MINNPAC membership. (2) Increasing the total number of members.

### Key Legislators Lose Races

The 1980 election took its toll on key friends of medicine. Senators Emily Staples, Doug Sillers, Dee Knaak and Emery Barrette lost their seats. Over on the House side, Representatives Bill Crandall, Jim Norman and Mike Fritz lost to the candidates they unseated in 1978. Also losing were Representatives Paul Thiede and Ray Kempe. In addition to these legislators several long time friends retired from the legislature in 1980. These include Senators Bob Dunn, George Perpich, Harm Ogdahl and Bill Kirchner and Representatives Ray Albrecht, Rod Searle and Ray Pleasant.

A bright note is the victory of Dr. Robert Reif who will return to serve a second term from the White Bear Lake area. Dr. Reif handily defeated his challenger winning 66% of the vote to return to his House seat.

With 23 new Senators and 25 new Representatives, the session will prove a challenge in educating these legislators on key medical issues. Certain to come before the next legislative session are bills relating to:

- (1) Chiropractors — expanding the scope of their practice to include blood drawing, and possibly more invasive procedures.
- (2) Optometrists — obtaining permission to use drugs during eye examinations.
- (3) HMOs — chiropractors and optometrists services to be mandatory components.
- (4) Third party reimbursement — nurses and other allied health practitioners obtaining direct reimbursement authorization.
- (5) Commitment proceedings — eroding physician input in the commitment process.

With DFL party control of both bodies (45 to 22 in the Senate; 70 to 64 in the House), it is expected that two veteran legislators will head up the health committees. Senator Sam Solon



## MINNPAC

of Duluth should succeed Senator George Perpich as chair of the Health, Welfare and Corrections Committee. Representative Jim Swanson, Richfield, should continue as chair of the Health and Welfare Committee.

### Future MINNPAC Board Activity

MINNPAC Board members will meet on December 12, 1980 to discuss membership for 1981 and review the recent election process. New board members meeting for the first time will be:

Gilbert Westreich, M.D.	Minneapolis
Keith H. Stolen, M.D.	Grand Rapids
Leslie A. Syverson, M.D.	Fergus Falls
Ardell W. Diessner, M.D.	Afton

### Other MINNPAC Board members are:

L. Ashley Whitesell, Jr., M.D.	Buffalo (Chairman)
Leon J. Nesvacil, M.D.	St. Paul (Treasurer)
Mr. David R. Adams	St. Paul
William Chandler, M.D.	Minneapolis
Roy Good, M.D.	Faribault
Jack Guy, M.D.	New London
Mrs. John (Mary) Harbaugh	St. Cloud
Mrs. Paul (Dottie) Hartzler	Cambridge
Mrs. Donald M. (Florence) Larson	Minneapolis
Stanley D. Mills, M.D.	Worthington
Robert J. Scheuerell, M.D.	St. Cloud
Robert Spencer, M.D.	Rochester
Thomas A. Stolee, M.D.	Duluth

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## MINNESOTA MEDICINE COVERS

Dr. Bruce Nydahl, Cover Editor, and the Board of Editors of MINNESOTA MEDICINE invite physicians to send in their 35 mm slides for possible covers for MINNESOTA MEDICINE. Slides of Minnesota, the seasons, and pieces of art, sculpture are particularly invited. However, we encourage you to send in slides of other areas or countries.

Identify each slide with your name and address and send the slides to MINNESOTA MEDICINE, 2221 University Avenue S.E., Suite 400, Minneapolis 55414.

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### Vail, Colorado: Medical Education Symposium

“Management of Common Office Problems”, January 18, 19, 20, 1981, 4 hours/day, Approved for Category I. For Brochure write: Medical Education Dept., St. Luke's Hospital, 915 East First Street, Duluth, Minnesota 55805.



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FAMILY PHYSICIAN needed to join a 10 member multi-specialty group in Southern Minnesota. Fairmont is a progressive city of 13,000 with excellent schools and recreational areas around a chain of five lakes. New 114 bed hospital adjacent to clinic. First year salary guaranteed with full partnership after one year. Contact Don Grandgenett, Fairmont Medical Clinic, PA Fairmont, MN 56031. (507) 238-4263.

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WANTED: Family practitioner, internist, OB-GYN to join multi-specialty group. One month vacation, hunting, fishing, and lake recreation area. Starting salary excellent: many fringe benefits included. Write Minnesota Medicine (704) 101 E. 5th St., St. Paul 55101.

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MINN. LOCUM TENENS availability Family Practice, can do OB. Board Certified FP's Aver. cost \$1800/week or \$300/24 hr plus Trans & Accom. Write Locum Tenens, 5695 Merry Lane Excelsior, MN 55331.

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PRIMARY CARE PHYSICIAN (F.P., I.M. or OB-Gyn) needed to join 3 physicians in West Central Minnesota resort community. Health facilities include 31-bed hospital, 74-bed nursing home and chemical dependency treatment program. Call or send C.V. to Richard Slieter, Ortonville Area Health Services, 750 Eastvold Ave., Ortonville, MN 56278. (612) 839-2525 or 6113.

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BIG LAKE, 40 MILES FROM MINNEAPOLIS needs and welcomes specialists willing to share office space: internal medicine/surgery/OB-GYN and other specialties, New clinic. Contact: S.K. Madireddi, M.D. at 425-2211.

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PRISON MEDICAL PRACTICE. Opportunity for Primary Care Physicians to join an academic program in prison medical group practice serving four unique institutions near the Twin City Metropolitan area. Affiliated with the Department of Medicine of a major teaching hospital, emphasis is placed on the development of progressive, comprehensive prison health care programs and a faculty appointment with the University of Minnesota Medical School. Good working conditions, competitive salary, and excellent benefits. For information write: Chairman, Department of Medicine, St. Paul Ramsey Medical Center, 640 Jackson Street, St. Paul, Minnesota 55101.

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*(Continued on page 902)*



## Classified Advertisements

(Continued from page 901)

**RHEUMATOLOGIST WANTED** — to join four Orthopedic Surgeons in very desirable North Central Wisconsin community with a drawing population of 70,000. Active practice assured, shared "on call" provided, research grants available. New clinic facility located within new 35 million dollar hospital complex. Outstanding personal benefit programs, generous guaranteed income. For further information contact: Lloyd Engstrom at (715) 842-3202, or write P.O. Box 1646, Wausau, Wis. 54401.

**GENERAL SURGEON** to join 11 member primary care group. 8 Family Physicians, 2 Internists and 1 General Surgeon. Recently remodeled and expanded clinic facility, 6 blocks from modern, well equipped 99 bed hospital. Rural Community 45 minutes south of the Metro area on 35-W. Salary guarantee first year. Contact: Darral Mischke, Clinic Administrator, Faribault Clinic, Ltd. 924 N.E. 1st Street, Faribault, Minnesota 55021.

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**WANTED — ORTHOPAEDIC SURGEON** board eligible or board qualified, to join busy two-man general orthopaedic practice in Alexandria, Minnesota. Please address correspondence to 111 17th Ave. E. Suite 100, Alexandria, Minnesota, 56308. Collect calls can be made to 612-762-1144.

**FAMILY PHYSICIAN** to join two Board-Certified family doctors, one physicians assistant, and one family counselor in a young and growing medical practice in beautiful Central Minnesota. The practice is oriented towards holistic medicine with a commitment to patient and community education. 80 minutes to downtown Minneapolis. Cultural and recreational activities in abundance. Salary depending on qualifications. Contact Adm. Daryl G. Mathews or Thomas J. Newton, M.D. at Cold Spring Medical Clinic, 26 N. Red River Ave., Cold Spring, MN 56320 — 612-685-8641.

**WANTED:** General surgeon for 17 physician multi-specialty group in Detroit Lakes, Minnesota. Physician-owned five-year-old clinic attached to a 100 bed hospital. First year salary with full participation in ownership negotiable at the end of one year. Fifty miles east of Fargo-Moorhead, in the Heart of the Lakes country. The area offers excellent recreational activities, with a top school system. Contact John R. Emery, M.D. or James F. Knapp, M.D. at Box 727, Detroit Lakes, MN 56501 or telephone (218) 847-3181.



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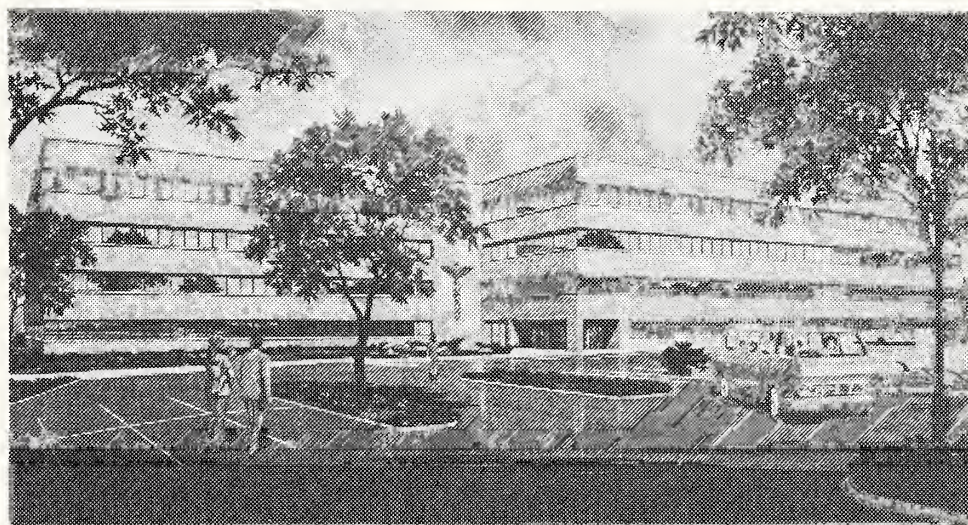
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**We Moved!**

The Minnesota Medical Association and MINNESOTA MEDICINE moved into the new Health Association Center on October 9th. The Address is:

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